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SESSION RESUMED IN FILE 'USPATFULL' AT 09:58:18 ON 23 JUL 2003
FILE 'USPATFULL' ENTERED AT 09:58:18 ON 23 JUL 2003
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	7.33	7.54

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.60	8.81

FILE 'USPATFULL' ENTERED AT 09:58:42 ON 23 JUL 2003
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Jul 2003 (20030722/PD)
FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)
HIGHEST GRANTED PATENT NUMBER: US6598233
HIGHEST APPLICATION PUBLICATION NUMBER: US2003135906
CA INDEXING IS CURRENT THROUGH 22 Jul 2003 (20030722/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Jul 2003 (20030722/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
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This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s rosiglitazone and maleate
415 ROSIGLITAZONE
36651 MALEATE
L4 165 ROSIGLITAZONE AND MALEATE

=> s l4 and pd<1997

2137014 PD<1997
(PD<19970000)
L5 1 L4 AND PD<1997

=> d l5 bib, ab, kwic

L5 ANSWER 1 OF 1 USPATFULL on STN
AN 2001:168152 USPATFULL
TI Substituted n-(indole-2-carbonyl-) amides and derivatives as glycogen phosphorylase inhibitors
IN Hulin, Bernard, Essex, CT, United States
Hoover, Dennis J., Stonington, CT, United States
Treadway, Judith L., Gales Ferry, CT, United States
Martin, William H., Essex, CT, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 6297269 B1 20011002
WO 9639385 19961212 <--
AI US 1997-952668 19971202 (8)
WO 1995-IB443 19950606
19971202 PCT 371 date
19971202 PCT 102(e) date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ramsuer, Robert W.; Assistant Examiner: Keating, Domenik
LREP Richardson, Peter C., Benson, Gregg C., Olson, A. Dean
CLMN Number of Claims: 77
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4318
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula I: ##STR1##

and their compositions are useful as glycogen phosphorylase inhibitors.
PI US 6297269 B1 20011002
WO 9639385 19961212 <--
SUMM . . . refers to nontoxic anionic salts containing anions such as (but not limited to) chloride, bromide, iodide, sulfate, bisulfate, phosphate, acetate, **maleate**, fumarate, oxalate, lactate, tartrate, citrate, gluconate, methanesulfonate and 4-toluene-sulfonate.
CLM What is claimed:
. . . effective amount of a.) 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl)-(2R)-hydroxy-3-oxo-propyl]-amide; b.) an antidiabetic agent selected from glypizide, glimepiride, repaglinide, metformin, pioglitazone, troglitazone, BRL49653 (**rosiglitazone**), acarbose and miglitol; and c.) optionally a pharmaceutically acceptable carrier.

74. A pharmaceutical composition as recited in claim 67 wherein the antidiabetic agent is BRL49653 (**rosiglitazone**).

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>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
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>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s 122320-73-4/rn
L1          148 122320-73-4/RN

=> l l1 and maleate
L IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l1 and maleate
         36651 MALEATE
L2           63 L1 AND MALEATE

=> s l2 and pd<1996
        2009397 PD<1996
                    (PD<19960000)
L3            2 L2 AND PD<1996

=> d l3 1-2 bib, ab, kwic

L3   ANSWER 1 OF 2  USPATFULL on STN
AN      96:120902  USPATFULL
TI      Heterocyclic compounds and their use in the treatment of Type-II
        diabetes
IN      Haigh, David, Horsham, England
PA      SmithKline Beecham PLC, Brentford, England (non-U.S. corporation)
PI      US 5589492              19961231
        WO 9321166  19931028                                          <--
AI      US 1994-318615          19941212 (8)
        WO 1993-GB735           19930407
                                19941212  PCT 371 date
                                19941212  PCT 102(e) date
PRAI    GB 1992-8016      19920410
        GB 1992-8451      19920416
        GB 1992-27046     19921229
DT      Utility
FS      Granted
EXNAM   Primary Examiner: Northington-Davis, Zinna
LREP    Stein-Fernandez, Nora, King, William T., Lentz, Edward T.
CLMN    Number of Claims: 12
ECL     Exemplary Claim: 1
DRWN    No Drawings
LN.CNT 1827
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      A compound of the formula A.sup.1 --X--(CH.sub.2).sub.n --O--A.sup.2
        --A.sup.3 --CO.R.sup.2 (I) or a tautomeric form thereof and/or a
        pharmaceutically acceptable salt thereof, and/or a pharmaceutically
        acceptable solvate thereof, wherein: A.sup.1 represents a substituted or
        unsubstituted aromatic heterocyclyl group; A.sup.2 represents a benzene
        ring having three optional substituents; A.sup.3 represents a moiety of
```

formula --(CH.sub.2).sub.m --CHR.sup.1 -- wherein R.sup.1 represents a halogen atom or a moiety of formula S(O).sub.p A.sup.4 wherein A.sup.4 represents hydrogen, substituted or unsubstituted alkyl, aryl, aralkyl, alkylcarbonyl or an aromatic heterocyclyl group and p represents zero or an integer 1 or 2 and m represents zero or an integer in the range of from 1 to 5, or A.sup.3 represents a moiety of formula --CH.dbd.CR.sup.1 -- wherein R.sup.1 is as defined above; R.sup.2 represents OR.sup.3 wherein R.sup.3 represents hydrogen, alkyl, aryl or aralkyl, or R.sup.2 represents --NR.sup.4 R.sup.5 wherein R.sup.4 and R.sup.5 each independently represent hydrogen or alkyl or R.sup.4 and R.sup.5 together with the nitrogen atom to which they are attached form a heterocyclic ring; X represents O, S or NR wherein R represents a hydrogen atom, an alkyl group, an acyl group, an aralkyl group wherein the aryl moiety may be substituted or unsubstituted, or a substituted or unsubstituted aryl group; and n represents an integer in the range of from 2 to 6; a process for the preparation of such a compound, a pharmaceutical composition comprising such a compound and the use of such a compound and composition in medicine.

PI US 5589492 19961231
WO 9321166 19931028 <--

SUMM . . . as the sulphate, nitrate, phosphate, borate, hydrochloride and hydrobromide and pharmaceutically acceptable organic acid addition salts such as acetate, tartrate, **maleate**, citrate, succinate, benzoate, ascorbate, methane-sulphonate, .alpha.-keto glutarate and .alpha.-glycerophosphate.

IT 5927-18-4, Trimethyl phosphonoacetate **122320-73-4** 122321-03-3
(reactant for [[[(pyridyl)amino]alkoxy]phenyl]alkanoate antidiabetic)

L3 ANSWER 2 OF 2 USPATFULL on STN
AN 95:114766 USPATFULL
TI Use of thiazolidinedione derivatives and related antihyperglycemic agents in the treatment of impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent diabetes mellitus
IN Olefsky, Jerrold, Solano Beach, CA, United States
Antonucci, Tammy, Mequon, WI, United States
Lockwood, Dean, Ann Arbor, MI, United States
Norris, Rebecca, Kewadin, MI, United States
PA Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI US 5478852 19951226 <--
AI US 1994-293899 19940823 (8)
RLI Continuation-in-part of Ser. No. US 1993-122251, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Frishauf, Holtz, Goodman, Langer & Chick
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1177
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel methods of using thiazolidinone derivatives and related antihyperglycemic agents to treat populations experiencing impaired glucose intolerance in order to prevent or delay the onset of noninsulin-dependent diabetes mellitus (NIDDM) and complications arising therefrom are disclosed.

PI US 5478852 19951226 <--

SUMM . . . nitrate, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, trifluoroacetate, propionate, caprylate, isobutyrate, oxalate, malonate, succinate, suberate, sebacate, fumarate, **maleate**, mandelate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate,

benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate, **maleate**, tartrate, methanesulfonate, and the like. Also contemplated are salts of amino acids such as arginate and the like and gluconate,. . .

IT 74772-77-3, Ciglitazone 87858-57-9 97322-87-7, Troglitazone 103787-97-9 109229-58-5, Englitazone 111025-46-8, Pioglitazone 118384-10-4 119670-18-7 122320-46-1 **122320-73-4** 125734-02-3 127810-37-1 134539-13-2 134868-21-6 141109-81-1 141200-24-0 142649-73-8 143811-62-5 173043-30-6
(thiazolidinedione derivs. in prevention of onset of noninsulin-dependent diabetes)

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NEWS 4	Feb 24	TEMA now available on STN
NEWS 5	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 6	Feb 26	PCTFULL now contains images
NEWS 7	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 8	Mar 24	PATDPAFULL now available on STN
NEWS 9	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 10	Apr 11	Display formats in DGENE enhanced
NEWS 11	Apr 14	MEDLINE Reload
NEWS 12	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 13	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 14	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 15	Apr 28	RDISCLOSURE now available on STN
NEWS 16	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 17	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 18	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
NEWS 20	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 21	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 22	Jun 06	PASCAL enhanced with additional data
NEWS 23	Jun 20	2003 edition of the FSTA Thesaurus is now available
NEWS 24	Jun 25	HSDB has been reloaded
NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 14:53:40 ON 22 JUL 2003

=> file uspatfull
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'USPATFULL' ENTERED AT 14:53:52 ON 22 JUL 2003
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Jul 2003 (20030722/PD)
FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)
HIGHEST GRANTED PATENT NUMBER: US6598233
HIGHEST APPLICATION PUBLICATION NUMBER: US2003135906
CA INDEXING IS CURRENT THROUGH 22 Jul 2003 (20030722/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Jul 2003 (20030722/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

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>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s thiazolidine-2,4-dione
          4459 THIAZOLIDINE
       3519997 2
       3466933 4
         19957 DIONE
L1         864 THIAZOLIDINE-2,4-DIONE
                 (THIAZOLIDINE(W)2(W)4(W)DIONE)

=> s  benzyl(1w)thiazolidine-2,4-dione
        139295 BENZYL
          4459 THIAZOLIDINE
       3519997 2
       3466933 4
         19957 DIONE
           864 THIAZOLIDINE-2,4-DIONE
```

```
                (THIAZOLIDINE(W)2(W)4(W)DIONE)
L2          172 BENZYL(1W)THIAZOLIDINE-2,4-DIONE

=> s ethoxy(1w)benzyl(1w)thiazolidine-2,4-dione
         77380 ETHOXY
        139295 BENZYL
          4459 THIAZOLIDINE
       3519997 2
       3466933 4
         19957 DIONE
           864 THIAZOLIDINE-2,4-DIONE
                 (THIAZOLIDINE(W)2(W)4(W)DIONE)
L3          105 ETHOXY(1W)BENZYL(1W)THIAZOLIDINE-2,4-DIONE

=> s l3 and pyridyl
         39467 PYRIDYL
L4           87 L3 AND PYRIDYL

=> s ;4 and N(1w)methyl
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):s ;4 and N(1w)methylend
       2429032 S
       3466933 4
         28779 S ;4
                 (S(W)4)
       1117304 N
             3 METHYLEND
             0 N(1W)METHYLEND
L5           0 S ;4 AND N(1W)METHYLEND


4 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
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"HELP COMMANDS" at an arrow prompt (=>).

=> s l4 and N(1w)methyl
       1117304 N
        404019 METHYL
         80700 N(1W)METHYL
L6          73 L4 AND N(1W)METHYL

=> s l6 and amino
        264308 AMINO
L7          72 L6 AND AMINO

=> s l7 and 2(1w) pyridyl
       3519997 2
         39467 PYRIDYL
         15076 2(1W) PYRIDYL
L8          65 L7 AND 2(1W) PYRIDYL

=> s l8 (1P) insulin
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L8 (1P) INSULIN'
         30490 INSULIN
L9          56 L8 (1P) INSULIN

=> d 18 1-3 bib, kwic

L8   ANSWER 1 OF 65  USPATFULL on STN
AN     2003:181525  USPATFULL
TI     Pharmaceutical compositions containing thiazolidinedione derivatives and
```

process for their preparation
IN Buckingham, Robin Edwin, Harlow, UNITED KINGDOM
Urquhart, Michael, Tonbridge, UNITED KINGDOM
PA SmithKline Beecham p.l.c. (non-U.S. corporation)
PI US 2003125358 A1 20030703
AI US 2003-358576 A1 20030205 (10)
RLI Continuation of Ser. No. US 2002-49917, filed on 19 Feb 2002, ABANDONED A 371 of International Ser. No. WO 2000-EP7926, filed on 14 Aug 2000, UNKNOWN
PRAI GB 1999-19465 19990817
GB 1999-19842 19990820
GB 1999-20149 19990825
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 664
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0009] One particular thiazolidinedione disclosed in EP 0306228 is 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** (hereinafter `Compound (I)`).
WO94/05659 discloses certain salts of Compound (I) including the maleate salt.
SUMM . . . thereof and/or a pharmaceutically acceptable salt thereof and/or a pharmaceutically acceptable solvate thereof; providing that formula (I) does not encompass 5-(4-{2-[(5-hydroxy-pyridin-2-yl)-methyl-**amino**]-**ethoxy**}-**benzyl**)-**thiazolidine-2,4-dione** and/or providing formula (I) does not encompass sulfuric acid mono-[6-({2-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-ethyl}-methyl-**amino**)-pyridin-3-yl ester.
SUMM [0094] Procedure 3. 6-{[2-(tert-butyl-dimethyl-silanyloxy)-ethyl]-methyl-**amino**}-pyridin-3-ol ##STR8##
SUMM [0105] Procedure 4. 2-[(5-Benzyloxy-pyridin-2-yl)-methyl-**amino**]-ethanol ##STR9##
SUMM [0115] Procedure 5: 5-(4-{2-[(5-Benzyloxy-pyridin-2-yl)-methyl-**amino**]-ethoxy}-benzylidene)-thiazolidine-2,4-dione ##STR10##
SUMM [0124] Procedure 6: 5-(4-{2-[(5-Benzyloxy-pyridin-2-yl)-methyl-**amino**]-**ethoxy**}-**benzyl**)-**thiazolidine-2,4-dione** ##STR11##
DETD 5-(4-{2-[(5-Hydroxy-pyridin-2-yl)-methyl-**amino**]-**ethoxy**}-**benzyl**)-**thiazolidine-2,4-dione**
DETD Sulfuric acid mono-[6-({2-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-ethyl}-methyl-**amino**)-pyridin-3-yl ester
CLM What is claimed is:
6. A composition according to claim 1, wherein the compound of formula (I) is 5-(4-{2-[(5-hydroxy-pyridin-2-yl)-methyl-**amino**]-**ethoxy**}-**benzyl**)-**thiazolidine-2,4-dione** or sulfuric acid mono-[6-({2-[4-(2,4-dioxo-thiazolidin-5-ylmethyl)-phenoxy]-ethyl}-methyl-**amino**)pyridin-3-yl ester; or a tautomeric form thereof and/or a pharmaceutically acceptable salt thereof, and/or a pharmaceutically acceptable solvate thereof,

L8 ANSWER 2 OF 65 USPATFULL on STN
AN 2003:174230 USPATFULL
TI 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)

amino)ethoxy]benzyl]thiazolidine-
2,4-dione, maleic acid salt, hydrate as
pharmaceutical
IN Sasse, Michael John, Tunbridge Wells, UNITED KINGDOM
Blackler, Paul David James, Tonbridge, UNITED KINGDOM
Lee, David C., Linton, UNITED KINGDOM
PA SmithKline Beecham plc (non-U.S. corporation)
PI US 2003120078 A1 20030626
AI US 2002-321055 A1 20021217 (10)
RLI Continuation of Ser. No. US 2002-82879, filed on 26 Feb 2002, ABANDONED
Continuation of Ser. No. US 2000-581826, filed on 16 Jun 2000, ABANDONED
A 371 of International Ser. No. WO 1998-EP8155, filed on 14 Dec 1998,
UNKNOWN
PRAI GB 1997-26566 19971216
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P.O. Box
1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 403
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)
amino)ethoxy]benzyl]thiazolidine-
2,4-dione, maleic acid salt, hydrate as
pharmaceutical
AB A hydrate of 5-[4-[2-(**N-methyl**-N-(**2-**
pyridyl)amino)ethoxy]benzyl]
thiazolidine-2, 4-dione, maleic
acid salt, characterised in that it: (i) comprises water in the range of
from 0.4 to 2.5 % w/w;. . .
SUMM [0002] International Patent Application, Publication Number WO94/05659
discloses certain thiazolidinedione derivatives having hypoglycaemic and
hypolipidaemic activity including 5-[4-[2-(**N-methyl**
-N-(2-pyridyl)amino)ethoxy]
benzyl]thiazolidine-2,4-
dione, maleic acid salt (hereinafter also referred to as
"Compound (I)").
SUMM [0005] Accordingly, the present invention provides a novel form of
5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)
amino)ethoxy]benzyl]thiazolidine-
2,4-dione, maleic acid salt (the "Hydrate")
characterised in that the Hydrate:
SUMM [0020] The invention also provides a process for preparing the Hydrate,
characterised in that 5-[4-[2-(**N-methyl**-N-(**2**
-pyridyl)amino)ethoxy]benzyl]
thiazolidine-2,4-dione, maleic
acid salt is crystallised from ethanol, suitably denatured ethanol,
containing 15 to 25% by volume of water, for example. . .
DETD Preparation of the Hydrate of 5-[4-[2-(**N-methyl**-N-(
2-pyridyl)amino)ethoxy]
benzyl]thiazolidine-2,4-
dione, Maleic Acid Salt
DETD [0050] 5-[4-[2-(**N-methyl**-N-(**2-**
pyridyl)amino)ethoxy]benzyl]
thiazolidine-2,4-dione free base
(6.0 g) and maleic acid salt (2.1 g, 1.05 molar equivalents) were heated
in methanol (40 ml) to. . .
DETD [0051] The Hydrate of 5-[4-[2-(**N-methyl**-N-(**2**
-pyridyl)amino)ethoxy]benzyl]
thiazolidine-2,4-dione, Maleic

Acid Salt was Also Prepared by Means of the Following Procedures:

DETD [0052] 5-[4-[2-(**N-Methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** (1.5 g, 4.2 mmole) and maleic acid (0.525 g@97.6% assay, 4.4 mmole, 1.05 mole equivalents) were heated in methanol (15. . . filtered and then cooled to 0.degree. C. with magnetic stirring at which point a thick suspension was formed. The product, 5-[4-[2-(**N-Methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** maleate, was isolated, washed with methanol and dried, in vacuo, at 52.degree. C. (Yield 1.4 g, 70.5%). Water content of. . .

DETD [0053] 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** free base (6.0 g) and maleic acid (2.1 g, 1.05 molar equivalents) were heated in acetonitrile (60 ml) containing water. . .

DETD [0054] The maleate salt of 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** anhydrate (3.0 g) was heated to 80.degree. C. in water (200 ml), then filtered hot and cooled to 20-25.degree. C.. . .

DETD [0055] The maleate salt of 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)ethoxy]benzyl]thiazolidione-2,4-dione anhydrate (2.0 g) was heated to 75.degree. C. in ethyl acetate (100 ml) containing water (3 ml), then filtered hot. . .

DETD [0056] 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** free base (6.0 g) and maleic acid (2.1 g, 1.05 molar equivalents) were heated in denatured ethanol (60 ml) containing. . .

CLM What is claimed is:

1. A hydrate of 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione**, maleic acid salt characterised in that it: (i) comprises water in the range of from 0.4 to 2.5% w/w; and. . .

11. A process for preparing a hydrate according to claim 1, characterised in that 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**)**amino**)**ethoxy**]**benzyl**]**thiazolidine-2,4-dione**, maleic acid salt is crystallised from ethanol containing 15 to 25% by volume of water.

L8 ANSWER 3 OF 65 USPATFULL on STN
AN 2003:161964 USPATFULL
TI Use of troglitazone and related compounds for the treatment of cancer
IN Urban, Randall J., Friendswood, TX, United States
Green, Allan, Galveston, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 6579893 B1 20030617
AI US 1998-102164 19980622 (9)
RLI Division of Ser. No. US 1997-811419, filed on 4 Mar 1997, now patented, Pat. No. US 5814647 Continuation of Ser. No. US 1998-102614, filed on 22 Jun 1998, now patented, Pat. No. US 6019947
DT Utility
FS GRANTED
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Arnold White & Durkee
CLMN Number of Claims: 25

ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . isoforms of PPAR.gamma. also exist, PPAR.gamma.1 and PPAR.gamma.2 (Vidal-Puig et al., 1996). These 2 proteins differ only in their NH.sub.2-terminal-30 **amino** acids and are the result of alternative promoter usage and differential mRNA splicing (Vidal-Puig et al., 1996). In addition to. . .

SUMM Z is hydrogen, (C.sub.1-C-)alkyl, (C.sub.1-C-)cycloalkyl, phenyl, naphthyl, **pyridyl**, furyl, thienyl, or phenyl momo- or disubstituted with the same or different groups which arc (C.sub.1-C.sub.3)alkyl, trifluoromethyl, (C.sub.1-C.sub.3)alkoxy, fluoro, chloro,. . .

SUMM Suitable values for A.sup.6 when it represents a 6-membered aromatic heterocyclyl group include **pyridyl** or pyrimidinyl. ##STR12##

SUMM Suitable values for A.sup.1 when it represents a 6-membered aromatic heterocyclyl group include **pyridyl** or pyrimidinyl.

DETD . . . R.sup.6 represents an aromatic acyl group, the aromatic moiety thereof may optionally have one or more substituents (for example, nitro, **amino**, alkylamino, dialkylamino, alkoxy, halo, alklyl, or hydroxy substituents); examples of such aromatic acyl groups included the benzoyl, p-nitrobenzoyl, m-fluorobenzoyl, o-. . .

DETD . . . carbon-carbon double or triple bonds and the aryl moiety thereof may optionally have one or more substituents (for example, nitro, **amino**, alkylamino, dialkylamino, alkoxy, halo, alkyl, or hydroxy substituents); examples of such araliphatic acyl groups include the phenylacetyl, p-chlorophenylacetyl, phenylpropionyl, and. . .

DETD Z is an oxygen atom or an **amino** group, most preferably an oxygen atom; and

DETD Referring to the general Formula II, the substituents may be any from 1 to 3 selected from nitro, **amino**, alkylamino, dialkylamino, alkoxy, halo, alkyl, or hydroxy, the aromatic acyl group may be benzoyl and naphthoyl. The alkyl group R.sup.11. . . mentioned 5- or 6-membered groups each including 1 or 2 hetero-atoms selected from among nitrogen, oxygen, and sulfur, such as **pyridyl**, thienyl, furyl, thiazolyl, etc. When R is ##STR19##

DETD . . . phenyl, optionally substituted with up to 5, preferably up to 3, groups selected from halogen, alkyl, phenyl, alkoxy, haloalkyl, hydroxy, **amino**, nitro, carboxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkylcarbonyloxy, or alkylcarborlyl groups.

DETD 5-[4-[2-[2,4dioxo-5-phenylthiazolidine-3-yl)**ethoxy**] **benzyl**]**thiazolidine-2,4-dione;**

DETD 5-[4-[2-[(**N-methyl**-N-(phenoxycarbonyl)**amino**]**ethoxy**]**benzyl**]**thiazolidine-2, 4-dione;**

DETD 5-[4-[2-(N-benzoxazol-2-yl)-N-metholamino]**ethoxy**] **benzyl**]**thiazolidine-2,4-dione;**

DETD 5-[4-[2-(**N-methyl**-N-(**2-pyridyl**) **amino**]**ethoxy**]**benzyl**]**thiazolidine-2,4-dione** (BRL 49653); and

DETD . . . chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate, benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate, maleate, tarirate, methanesulfonate, and the like. Also contemplated are salts of **amino** acids such as arginate and the like and gluconate, galacturonate, **n-methyl** glucamine (see, for example, Berge et al., 1977).

CLM What is claimed is:

. . . X is S, O, NR.sub.18, --CH.dbd.N or --N.dbd.CH Y is CH or N; Z is

hydrogen, (C.sub.1-C.sub.7)alkyl, (C.sub.3-C.sub.7)cycloalkyl, phenyl, naphthyl, **pyridyl**, furyl, thienyl, or phenyl mono- or disubstituted with the same or different groups which are (C.sub.1-C.sub.3)alkyl, trifluoromethyl, (C.sub.1-C.sub.3)alkoxy, fluoro, chloro,. . .

. . . administering to the subject a therapeutically effective amount of a compound selected from the group consisting of: (.+-.)-5-{{4-{(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy}phenyl}methyl}-2,4-thiazolidinedione: (troglitazone); 4-(2-naphthylmethyl)-1,2,3,5-oxathiadiazole-2-oxide; 5-{4-{2-{2,4-dioxo-5-phenylthiazolidin-3-yl)**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{4-{2-{**N-methyl**-N-(phenoxycarbonyl)**amino**}**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{4-(2-phenoxyethoxy)benzyl}thiazolidine-2,4-dione; 5-{4-{2-(4-chlorophenyl)ethylsulfonyl}benzyl}thiazolidine-2,4-dione; 5-{4-{3-(5-methyl-2-phenyloxazol-4-yl)propionyl}benzyl}thiazolidine-2,4-dione; 5-{4-{(1-methylcyclohexyl)methoxy}benzyl}thiazolidine-2,4-dione: (ciglitazone); 5-{{4-(3-hydroxyl-methylcycloxhexyl)methoxy}benzyl}thiazolidine-2,4-dione; 5-{4-{2-(5-methyl-2-phenyloxazol-4-yl)**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{4-{2-(5-ethylpyridin-2-yl)**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**: (pioglitazone); 5-{(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl}thiazolidine-2,4-dione: (englitazone); 5-{{2-(2,-naphthylmethyl)benzoxazol}-5-ylmethyl}thiazolidine-2,4-dione; 5-{4-{2-(2-phenylureido)**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{4-{2-{N-(benzoxazol-2-yl)-N-methylamino}**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{4-{2-{2,4-dioxo-5-phenylthiazolidin-3-yl)**ethoxy**}**benzyl**}**thiazolidine-2,4-dione**; 5-{2-(5-methyl-2-penyloxazol-4-ylmethyl)benzofuran-5-ylmethyl}-oxazolidine-2,4-dione; 5-{4-{2-{**N-methyl**-N-(**2-pyridyl**)**amino**}**ethoxy**}**benzyl**}**thiazolidine-2,4-dione** (BRL49653); and 5-{4-{2-{N-(benzoxazol-2-yl)-N-methylamino}ethoxy}benzyl}oxazolidine-2,4-dione.

=> file registry

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	21.69	21.90

FILE 'REGISTRY' ENTERED AT 15:02:41 ON 22 JUL 2003

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 JUL 2003 HIGHEST RN 552272-14-7
DICTIONARY FILE UPDATES: 21 JUL 2003 HIGHEST RN 552272-14-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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=> s BNL49653/CN
L10           0 BNL49653/CN

=> s BNL 49653/CN
L11           0 BNL 49653/CN

=> s BRL 49653/CN
L12           1 BRL 49653/CN

=> D L12

L12  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS on STN
RN   122320-73-4  REGISTRY
CN   2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
     hyl]- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   5-[4-[2-(N-Methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione
CN   BRL 49653
CN   Rosiglitazone
FS   3D CONCORD
MF   C18 H19 N3 O3 S
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
       BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
       EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)
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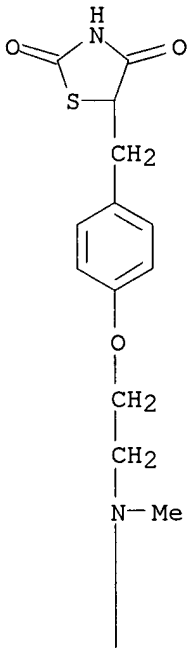
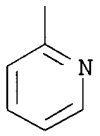
PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

604 REFERENCES IN FILE CA (1947 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
620 REFERENCES IN FILE CAPLUS (1947 TO DATE)

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.34	38.24

FILE 'USPATFULL' ENTERED AT 15:05:33 ON 22 JUL 2003

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 22 Jul 2003 (20030722/PD)
FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)
HIGHEST GRANTED PATENT NUMBER: US6598233
HIGHEST APPLICATION PUBLICATION NUMBER: US2003135906
CA INDEXING IS CURRENT THROUGH 22 Jul 2003 (20030722/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 22 Jul 2003 (20030722/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2003

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>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
>>>  publication date for all the US publications for an invention     <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL   <<<
>>>  records and may be searched in standard search fields, e.g., /PN, <<<
>>>  /PK, etc.                                                         <<<

>>>  USPATFULL and USPAT2 can be accessed and searched together        <<<
>>>  through the new cluster USPATALL.  Type FILE USPATALL to          <<<
>>>  enter this cluster.                                               <<<
>>>                                                                    <<<
>>>  Use USPATALL when searching terms such as patent assignees,       <<<
>>>  classifications, or claims, that may potentially change from      <<<
>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s rosiglitazone (1p) insulin
           415 ROSIGLITAZONE
         30490 INSULIN
L13        285 ROSIGLITAZONE (1P) INSULIN

=> s l13 nd pd<1994
MISSING OPERATOR L13 ND
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

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L14          0 L13 AND PD<1994

=> s l13 and pd<1995
       1890730 PD<1995
                 (PD<19950000)
L15          0 L13 AND PD<1995

=> s l13 and pd<1995
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L16          0 L13 AND PD<1995

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L18          0 L13 AND PD<1997

=> s l13 and pd<1998
       2268411 PD<1998
                 (PD<19980000)
L19          0 L13 AND PD<1998
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=> d l13 1-5

L13 ANSWER 1 OF 285 USPATFULL on STN
AN 2003:195245 USPATFULL
TI Imidazole compounds
IN Andersen, Knud Erik, Brondby, DENMARK
Dorwald, Florencio Zaragoza, Ballerup, DENMARK
Peschke, Bernd, Malov, DENMARK
Sidelmann, Ulla Grove, Vedbaek, DENMARK
Rudolf, Klaus, Warthausen, GERMANY, FEDERAL REPUBLIC OF
Stenkamp, Dirk, Biberach, GERMANY, FEDERAL REPUBLIC OF
Hurnaus, Rudolf, Biberach, GERMANY, FEDERAL REPUBLIC OF
Muller, Stephan Georg, Warthausen, GERMANY, FEDERAL REPUBLIC OF
Krist, Bernd, Ulm, GERMANY, FEDERAL REPUBLIC OF
Eriksen, Birgitte, Farum, DENMARK
PI US 2003135056 A1 20030717
AI US 2002-201865 A1 20020723 (10)
RLI Continuation of Ser. No. US 2001-810237, filed on 16 Mar 2001, GRANTED, Pat. No. US 6437147
PRAI DK 2000-441 20000317
DK 2000-1016 20000629
US 2000-193741P 20000331 (60)
US 2000-216553P 20000707 (60)
DT Utility
FS APPLICATION
LN.CNT 4775
INCL INCLM: 548/303.100
NCL NCLM: 548/303.100
IC [7]
ICM: C07D495-02

L13 ANSWER 2 OF 285 USPATFULL on STN
AN 2003:195079 USPATFULL
TI Antidiabetic 4-hydroxy-2-furoic acids
IN Chen, Shieh-Shung Tom, Morganville, NJ, UNITED STATES
Zhang, Bei B., Edison, NJ, UNITED STATES
Li, Xiaohua, Edison, NJ, UNITED STATES
PI US 2003134890 A1 20030717
US 6596760 B2 20030722
AI US 2002-274461 A1 20021018 (10)
PRAI US 2001-330291P 20011018 (60)
DT Utility
FS APPLICATION
LN.CNT 927
INCL INCLM: 514/414.000
INCLS: 548/454.000
NCL NCLM: 514/455.000
NCLS: 435/017.000; 548/455.000
IC [7]
ICM: A61K031-404
ICS: C07D045-14

L13 ANSWER 3 OF 285 USPATFULL on STN
AN 2003:195073 USPATFULL
TI Neovascularization inhibitors
IN Hazama, Masatoshi, Osaka, JAPAN
Miyazaki, Takeshi, Osaka, JAPAN
Sugiyama, Yasuo, Kawanishi-shi, JAPAN
PI US 2003134884 A1 20030717
AI US 2002-239749 A1 20020926 (10)
WO 2001-JP2447 20010327

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PRAI   JP 2000-92966       20000328
DT     Utility
FS     APPLICATION
LN.CNT 1660
INCL   INCLM: 514/367.000
       INCLS: 514/374.000; 514/567.000; 514/562.000; 514/357.000
NCL    NCLM:  514/367.000
       NCLS:  514/374.000; 514/567.000; 514/562.000; 514/357.000
IC     [7]
       ICM: A61K031-421
       ICS: A61K031-195; A61K031-44; A61K031-426

L13  ANSWER 4 OF 285  USPATFULL on STN
AN     2003:188542  USPATFULL
TI     Bis-Heteroaryl alkanes as therapeutic agents
IN     Mjalli, Adnan M. M., Jamestown, NC, UNITED STATES
       Shahbaz, Kathy G.J., Escondido, CA, UNITED STATES
PI     US 2003130335      A1   20030710
AI     US 2002-273795     A1   20021018 (10)
PRAI   US 2001-348187P     20011019 (60)
DT     Utility
FS     APPLICATION
LN.CNT 1731
INCL   INCLM: 514/414.000
       INCLS: 548/455.000
NCL    NCLM:  514/414.000
       NCLS:  548/455.000
IC     [7]
       ICM: A61K031-404
       ICS: C07D043-02

L13  ANSWER 5 OF 285  USPATFULL on STN
AN     2003:188513  USPATFULL
TI     Substituted acid derivatives useful as antidiabetic and antiobesity
       agents and method
IN     Devasthale, Pratik, Plainsboro, NJ, UNITED STATES
       Jeon, Yoon T., Belle Mead, NJ, UNITED STATES
PI     US 2003130306      A1   20030710
AI     US 2002-289053     A1   20021106 (10)
PRAI   US 2001-333022P     20011106 (60)
DT     Utility
FS     APPLICATION
LN.CNT 1699
INCL   INCLM: 514/301.000
       INCLS: 514/302.000; 514/303.000; 546/113.000; 546/114.000; 546/115.000
NCL    NCLM:  514/301.000
       NCLS:  514/302.000; 514/303.000; 546/113.000; 546/114.000; 546/115.000
IC     [7]
       ICM: C07D491-02
       ICS: C07D498-02; C07D471-02; A61K031-4745; A61K031-4743; A61K031-4741


=> s l13 and pd<2000
       2606853 PD<2000
                 (PD<20000000)
L20           4 L13 AND PD<2000

=> d l20 1-4 bib, kwic

L20  ANSWER 1 OF 4  USPATFULL on STN
AN     2001:226644  USPATFULL
TI     Amine compounds, their production and use
```

IN Suzuki, Nobuhiro, Tsukuba, Japan
Kato, Kaneyoshi, Kawanishi, Japan
Takekawa, Shiro, Tsukuba, Japan
Terauchi, Jun, Ikeda, Japan
Endo, Satoshi, Takatsuki, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6329389 B1 20011211
WO 9952875 19991021 <--
AI US 1999-424285 19991119 (9)
WO 1999-JP1871 19990408
19991119 PCT 371 date
19991119 PCT 102(e) date
PRAI JP 1998-96422 19980408
JP 1998-345328 19981204
DT Utility
FS GRANTED
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Philippe Y. Riesen, Chao, Mark
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6360
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6329389 B1 20011211
WO 9952875 19991021 <--
SUMM . . . "prevention or treatment of diseases or symptoms caused by insufficiency of growth hormone or IGF-1" includes, for example, treatment of **insulin**-dependent and non-**insulin** dependent diabetes mellitus or a variety of diseases associated with them, namely diabetic complications such as diabetic retinopathy, diabetic nephropathy,. . . In the treatment of diabetes mellitus or diseases associated with them, other antidiabetic agents (e.g., thiazolidinediones such as Troglitazone, pioglitazone, **Rosiglitazone**, and etc.; glucagon antagonists; glucose absorption inhibitors such as acarbose, and etc) can be used concomitantly. Further, r other hormones. . .

L20 ANSWER 2 OF 4 USPATFULL on STN
AN 2001:97948 USPATFULL
TI Oxyiminoalkanoic acid derivatives with hypoglycemic and hypolipidemic activity
IN Momose, Yu, Takarazuka, Japan
Odaka, Hiroyuki, Kobe, Japan
Imoto, Hiroshi, Kusatsu, Japan
Kimura, Hiroyuki, Sakai, Japan
Sakamoto, Junichi, Toyonaka, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6251926 B1 20010626
WO 9958510 19991118 <--
AI US 1999-423854 19991115 (9)
WO 1999-JP2407 19990510
19991115 PCT 371 date
19991115 PCT 102(e) date
PRAI JP 1998-127921 19980511
JP 1998-127922 19980511
DT Utility
FS GRANTED
EXNAM Primary Examiner: Powers, Fiona T.; Assistant Examiner: Wright, Sonya
LREP Riesen, Philippe Y.
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 5841
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6251926 B1 20010626
WO 9958510 19991118 <--
SUMM Examples of an agent for treating diabetes mellitus are an **insulin** formulation (e.g., animal **insulin** formulations extracted from a pancreas of a cattle or a swine; a human **insulin** formulation synthesized by a gene engineering technology using colibacillus and yeasts), an **insulin** sensitivity enhancing agent (e.g., pioglitazone hydrochloride, troglitazone, **rosiglitazone** and the like), an .alpha.-glycosidase inhibitor (e.g., voglibose, acarbose, miglitol, emiglitate and the like), a Biguanide (e.g., phenformin, metoformin, buformin. . . like), or a sulfonylurea (e.g., tolbutamide, glibenclamid, gliclazide, chlorpropamide, tolazamide, acetohexamide, glyclopyramide, glimepiride and the like) as well as other **insulin** secretion-promoting agents (e.g., repaglinide, senaglinide, nateglinide, mitiglinide, GLP-1 and the like), amyrin agonist (e.g. pramlintide and the like), phosphotyrosinphosphatase inhibitor. . .

L20 ANSWER 3 OF 4 USPATFULL on STN
AN 1999:132855 USPATFULL
TI Sulfonylurea-glitazone combinations for diabetes
IN Whitcomb, Randall Wayne, Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 5972973 19991026 <--
AI US 1998-173911 19981016 (9)
RLI Continuation-in-part of Ser. No. US 1997-970057, filed on 13 Nov 1997, now patented, Pat. No. US 5859037
PRAI US 1997-38224P 19970219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Ashbrook, Charles W.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 733
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5972973 19991026 <--
CLM What is claimed:
. . . 3 mg to about 250 mg of a sulfonylurea antidiabetic agent and about 5 mg to about 50 mg of **rosiglitazone** (BRL49653), said amounts of sulfonylurea and **rosiglitazone** being synergistic for the treatment of non-**insulin** dependent diabetes mellitus in humans.

3. A composition of claim 5 comprising **rosiglitazone** and glyburide.

4. A method of treating non-**insulin** dependent diabetes mellitus in humans comprising administering to a patient in need of treatment from about 3 mg to about 250 mg of a sulfonylurea antidiabetic agent in combination with about 5 mg to about 50 mg of **rosiglitazone**, said amounts of sulfonylurea and **rosiglitazone** being synergistic for the treatment of non-**insulin** dependent diabetes mellitus in humans.

6. A method of treating non-**insulin** dependent diabetes mellitus in humans comprising administering to a patient in need of treatment from about 3 mg to about 250 mg of a sulfonylurea antidiabetic

agent in combination with about 5 mg to about 10 mg of **rosiglitazone**, said amounts of sulfonylurea and **rosiglitazone** being synergistic for the treatment of non-**insulin** dependent diabetes mellitus in humans.

L20 ANSWER 4 OF 4 USPATFULL on STN
AN 1999:132827 USPATFULL
TI Use of thiazolidinedione derivatives in the treatment of anovulation, hyperandrogenism and hirsutism
IN Antonucci, Tammy, Thousand Oaks, CA, United States
Lockwood, Dean, Ann Arbor, MI, United States
Norris, Rebecca, Kewadin, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 5972944 19991026 <--
AI US 1998-124707 19980729 (9)
RLI Division of Ser. No. US 1997-868608, filed on 4 Jun 1997 which is a continuation-in-part of Ser. No. US 1997-856987, filed on 15 May 1997, now patented, Pat. No. US 5874454 which is a continuation-in-part of Ser. No. US 1996-763286, filed on 10 Dec 1996, now abandoned which is a division of Ser. No. US 1995-469398, filed on 6 Jun 1995, now patented, Pat. No. US 5602133 which is a division of Ser. No. US 1994-292585, filed on 23 Aug 1994, now patented, Pat. No. US 5457109 which is a continuation-in-part of Ser. No. US 1993-122251, filed on 15 Sep 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Reamer, James H.
LREP Ashbrook, Charles W.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1312
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5972944 19991026 <--
SUMM 5-(4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl)-2,4-thiazolidine (**Rosiglitazone**).
SUMM . . . is referred to as cardiovascular complications or several of the metabolic and circulatory disturbances that are associated with hyperglycemia, eg, **insulin** resistance, hyperinsulinemia and/or hyperproinsulinemia, delayed **insulin** release, dyslipidemia, retinopathy, peripheral neuropathy, nephropathy, and hypertension.

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=> s RN 122320-73-4
          9801 RN
             0 122320-73-4
L21          0 RN 122320-73-4
                 (RN(W)122320-73-4)

=> s  122320-73-4/RN
L22        148 122320-73-4/RN

=> S L22 AND INSULIN/CLS
'CLS' IS NOT A VALID FIELD CODE
             0 INSULIN/CLS
L23          0 L22 AND INSULIN/CLS

=> S L22 AND INSULIN/CLM
          4420 INSULIN/CLM
L24         78 L22 AND INSULIN/CLM
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=> S L24 AND PD<1999
       2435625 PD<1999
                  (PD<19990000)
L25           3 L24 AND PD<1999

=> D L25 BIB, KWIC

L25  ANSWER 1 OF 3  USPATFULL on STN
AN      1998:101666  USPATFULL
TI      Treatment of arteriosclerosis and xanthoma
IN      Tsujita, Yoshio, Tokyo, Japan
        Horikoshi, Hiroyoshi, Kobe, Japan
        Ito, Takashi, Kobe, Japan
PA      Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI      US 5798375              19980825                                <--
AI      US 1996-676090          19960702 (8)
PRAI    JP 1995-167291      19950703
DT      Utility
FS      Granted
EXNAM   Primary Examiner: Criares, Theodore J.
LREP    Frishauf, Holtz, Goodman, Langer & Chick, Esq.
CLMN    Number of Claims: 6
ECL     Exemplary Claim: 1
DRWN    No Drawings
LN.CNT 1158
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI      US 5798375              19980825                                <--
CLM     What is claimed is:
  . . .  agent selected from the group consisting of HMG-CoA reductase
        inhibitors and a second agent selected from the group consisting of
        insulin sensitizers, said first and second agents being
        administered together in a synergistic mixture or individually in
        amounts and within such a period as to act synergistically together;
        wherein said HMG-CoA reductase inhibitor is pravastatin and said
        insulin sensitizer is troglitazone.

IT     75330-75-5, Lovastatin   79902-63-9, Simvastatin   81093-37-0,
       Pravastatin   81131-70-6, Pravastatin sodium   93957-54-1, Fluvastatin
       97322-87-7, Troglitazone   109229-58-5, Englitazone   111025-46-8,
       Pioglitazone 122320-73-4, BRL-49653   134523-00-5, Atorvastatin
       143201-11-0, Rivastatin   178054-38-1   187220-90-2   187220-91-3
         (synergistic compn. contg. insulin sensitizer and HMG-CoA reductase
         inhibitor for treatment of arteriosclerosis)


=> D L25 2-3 BIB, KWIC

L25  ANSWER 2 OF 3  USPATFULL on STN
AN      1998:54924  USPATFULL
TI      Treatment and prophylaxis of pancreatitis
IN      Fujiwara, Toshihiko, Ebina, Japan
        Horikoshi, Hiroyoshi, Funabashi, Japan
        Fukami, Masaharu, Yokohama, Japan
PA      Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI      US 5753681              19980519                                <--
AI      US 1997-819686          19970317 (8)
PRAI    JP 1996-61063       19960318
        JP 1996-250201      19960920
DT      Utility
FS      Granted
EXNAM   Primary Examiner: Jordan, Kimberly
```

LREP Frishauf, Holtz, Goodman, Langer & Chick, P.C.
CLMN Number of Claims: 52
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1149
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5753681 19980519 <--
CLM What is claimed is:

. . . or prophylaxis of pancreatitis by administering to a human suffering from or susceptible to pancreatitis an effective dose of an **insulin** sensitizer sufficient to treat or inhibit pancreatitis.

2. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of thiazolidinedione compounds, oxazolidinedione compounds, isoxazolidinedione compounds and oxadiazolidinedione compounds.

3. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of thiazolidinedione compounds and isoxazolidinedione compounds.

4. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of compounds of formula (I): ##STR4## wherein: R.sup.1 and R.sup.2 are the same. . .

5. The method of claim 4, wherein said **insulin** sensitizer is selected from the group consisting of compounds of formula (Ia): ##STR5## wherein: R.sup.1, R.sup.2, R.sup.4 and R.sup.5 are. . .

34. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-hydroxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)-benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

35. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-hydroxy-2-methyl-7-t-butylchroman-2-ylmethoxy)-benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

36. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-hydroxy-2-ethyl-5,7,8-trimethylchroman-2-yl-methoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

37. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-hydroxy-2-isobutyl-5,7,8-trimethylchroman-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

38. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-acetoxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)-benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

39. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-ethoxycarbonyloxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

40. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[6-(2-fluorobenzyloxy)-2-naphthylmethyl] thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

41. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-{4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl}thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

42. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-(2-benzyl-3,4-dihydro-2H-benzopyran-6-ylmethyl)-thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

43. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-{2-[N-methyl-N-(pyridin-2-yl)amino]ethoxy}benzyl]-thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

44. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-(4-{2-[1-(4-2'-pyridylphenyl)ethylideneaminooxy]ethoxy}-benzyl)thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

45. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 4-{4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxy]benzyl}-isoxazolidine-3,5-dione and pharmaceutically acceptable salts thereof.

46. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-{4-(5-methoxy-3-methylimidazo[4,5-b]pyridin-2-yl-methoxy)benzyl}thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

47. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-{4-(5-methoxy-3-methylimidazo[4,5-b]pyridin-2-yl-methoxy)benzyl}thiazolidine-2,4-dione and its hydrochloride.

48. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

49. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

50. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

51. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-[4-(1-methylindolin-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

52. The method of claim 1, wherein said **insulin** sensitizer is selected from the group consisting of 5-{4-[3-(5-methyl-2-phenyloxazol-4-yl)propionyl]benzyl}thiazolidine-2,4-dione and pharmaceutically acceptable salts thereof.

IT 2295-31-0D, Thiazolidinedione, derivs. 12770-97-7D, Oxazolidinedione, derivs. 97322-87-7, Troglitazone 97322-88-8 97323-04-1 97323-05-2

109229-58-5, Englitazone 111025-46-8, Pioglitazone 115344-44-0D, 3,5-Isoxazolidinedione, derivs. **122320-73-4**, BRL-49653
137786-87-9 141200-24-0, Darglitazone 161600-01-7 170861-63-9
172647-49-3 178054-38-1 185428-14-2 185428-18-6 185428-23-3
187220-90-2 187220-91-3
(thiazolidinedione derivs. and other insulin sensitizers for pancreatitis treatment)

L25 ANSWER 3 OF 3 USPATFULL on STN
AN 1998:4611 USPATFULL
TI Use of thiazolidinedione derivatives and related antihyperglycemic agents in the treatment of insulin resistant subjects with normal glucose tolerance in order to prevent or delay the onset of noninsulin-dependent mellitus
IN Olefsky, Jerrold M., Solana Beach, CA, United States
PA Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI US 5708012 19980113 <--
AI US 1995-431266 19950428 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Cooney, Jr., John M.
LREP Frishauf, Holtz, Goodman, Langer & Chick, P.C.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1393
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5708012 19980113 <--
CLM What is claimed is:
1. A method of treating **insulin** resistant non-impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a. . .
9. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
13. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
14. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
15. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
16. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
17. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
18. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
19. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
20. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
21. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .

22. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
23. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
25. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .
26. A method of treating **insulin** resistant non-impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent diabetes mellitus comprising administering to a host suffering. . .

IT 74772-77-3, Ciglitazone 87858-57-9 97322-87-7, Troglitazone
103787-97-9 109229-58-5, Englitazone 111025-46-8, Pioglitazone
118384-10-4 119670-18-7 122320-46-1 **122320-73-4**
125734-02-3 127810-37-1 132646-45-8 134539-13-2 134868-21-6
141109-81-1 141200-24-0 142649-73-8 143811-62-5
(thiazolidinedione derivs. and related antihyperglycemic agents in treatment of insulin-resistant subjects with normal glucose tolerance to prevent or delay onset of noninsulin-dependent diabetes mellitus)

=> D HIS

(FILE 'HOME' ENTERED AT 14:53:40 ON 22 JUL 2003)

FILE 'USPATFULL' ENTERED AT 14:53:52 ON 22 JUL 2003
L1 864 S THIAZOLIDINE-2,4-DIONE
L2 172 S BENZYL(1W)THIAZOLIDINE-2,4-DIONE
L3 105 S ETHOXY(1W)BENZYL(1W)THIAZOLIDINE-2,4-DIONE
L4 87 S L3 AND PYRIDYL
L5 0 S S ;4 AND N(1W)METHYLEND
L6 73 S L4 AND N(1W)METHYL
L7 72 S L6 AND AMINO
L8 65 S L7 AND 2(1W) PYRIDYL
L9 56 S L8 (1P) INSULIN

FILE 'REGISTRY' ENTERED AT 15:02:41 ON 22 JUL 2003
L10 0 S BNL49653/CN
L11 0 S BNL 49653/CN
L12 1 S BRL 49653/CN

FILE 'USPATFULL' ENTERED AT 15:05:33 ON 22 JUL 2003
L13 285 S ROSIGLITAZONE (1P) INSULIN
L14 0 S L13 AND PD<1994
L15 0 S L13 AND PD<1995
L16 0 S L13 AND PD<1995
L17 0 S L13 AND PD<1996
L18 0 S L13 AND PD<1997
L19 0 S L13 AND PD<1998
L20 4 S L13 AND PD<2000
L21 0 S RN 122320-73-4
L22 148 S 122320-73-4/RN
L23 0 S L22 AND INSULIN/CLS
L24 78 S L22 AND INSULIN/CLM
L25 3 S L24 AND PD<1999

=> S L22 AND SYNERGIS?
48449 SYNERGIS?
L26 30 L22 AND SYNERGIS?

=> D L26 1-30 BIB, KWIC

L26 ANSWER 1 OF 30 USPATFULL on STN
AN 2003:166531 USPATFULL
TI Combination of organic compounds
IN Webb, Randy Lee, Flemington, NJ, UNITED STATES
PI US 2003114389 A1 20030619
AI US 2002-290651 A1 20021108 (10)
PRAI US 2001-350708P 20011113 (60)
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 430/2, EAST HANOVER, NJ, 07936-1080
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . or, in each case, a pharmaceutically acceptable form thereof, results not only in a beneficial, especially a potentiating or a **synergistic**, therapeutic effect. Independent thereof, additional benefits resulting from combined treatment can be achieved such as a surprising prolongation of efficacy,. . .
SUMM [0039] The term "**synergistic**" shall mean that the drugs, when taken together, produce a total joint effect that is greater than the sum of. . .
SUMM . . . structural or functional protein within the cardio-renal system. This effect proves to be highly beneficial by evoking an additive or **synergistic** effect on vascular function/structure when administered with the renin inhibitor of formula (I) which alone improves cardiovascular function and structure. . .
SUMM [0065] in particular a potentiation or a **synergism**, e.g. a more than additive effect, additional advantageous effects, less side effects, a combined therapeutical effect in a non-effective dosage of one or each of the components, especially a potentiation or a strong **synergism**.
IT 657-24-9, Metformin 105816-04-4, Nateglinide 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 135062-02-1, Repaglinide 145375-43-5, Mitiglinide 173334-57-1, Aliskiren 173334-58-2
(pharmaceutical compns. contg. renin inhibitor and antidiabetics)

L26 ANSWER 2 OF 30 USPATFULL on STN
AN 2003:134661 USPATFULL
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and alpha glucocidase inhibitor
IN Buckingham, Robin Edwin, Welwyn Garden City, UNITED KINGDOM
Smith, Stephen Alistair, Bramfield, UNITED KINGDOM
PA SmithKline Beecham p.l.c. (non-U.S. corporation)
PI US 2003092750 A1 20030515
AI US 2002-322982 A1 20021218 (10)
RLI Continuation of Ser. No. US 2001-989572, filed on 20 Nov 2001, ABANDONED
Continuation of Ser. No. US 1999-445908, filed on 15 Dec 1999, ABANDONED
A 371 of International Ser. No. WO 1998-GB2112, filed on 16 Jul 1998, UNKNOWN
PRAI GB 1997-15298 19970718
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 493
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0046] The particularly beneficial effect on glycaemic control provided by the treatment of the invention is indicated to be a **synergistic** effect relative to the control expected for the sum of the effects of the individual active agents.
IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 631-27-6, Glyclopyramide 664-95-9, Glycyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol 74772-77-3, Ciglitazone 80879-63-6, Emiglitate 93479-97-1, Glimepiride 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4** 135062-02-1, Repaglinide 155141-29-0
(thiazolidinedione, insulin secretagogue, and .alpha.-glucosidase inhibitor for diabetes treatment)

L26 ANSWER 3 OF 30 USPATFULL on STN
AN 2003:123367 USPATFULL
TI Method of treating metabolic disorders especially diabetes, or a disease or condition associated with diabetes
IN Gatlin, Marjorie Regan, Hoboken, NJ, United States
Ball, Michele Ann, Morris Plains, NJ, United States
Mannion, Richard Owen, Mount Arlington, NJ, United States
Karnachi, Anees Abdulquadar, Hillsborough, NJ, United States
Guitard, Christiane, Hegenheim, FRANCE
Allison, Malcolm, Basel, SWITZERLAND
PA Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)
PI US 6559188 B1 20030506
AI US 2000-663264 20000915 (9)
PRAI US 2000-304196P 20000407 (60)
US 2000-240918P 20000309 (60)
US 1999-242911P 19990917 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Thallemer, John D.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . at least one other antidiabetic compound selected from the group consisting of glitazones, sulfonyl ureas and metformin, in particular a **synergism**, e.g. a more than additive effect, additional advantageous effects, less side effects, a combined therapeutical effect in a non-effective dosage. . . one other antidiabetic compound selected from the group consisting of glitazones, sulfonyl urea derivatives and metformin, and especially a strong **synergism** between nateglinide or repaglinide and at least one other antidiabetic compound selected from the group consisting of glitazones, sulfonyl urea. . .
SUMM . . . one beneficial effect, e.g. a mutual enhancing of the effect of nateglinide and the antidiabetic thiazolidinedione derivative, in particular a **synergism**, e.g. a more than additive effect, additional advantageous effects, less side effects, a combined therapeutical effect in a non-effective dosage of one or each of the components nateglinide and the antidiabetic thiazolidinedione derivative, especially a strong **synergism** between nateglinide and the anti-diabetic thiazolidinedione derivative.

SUMM . . . glitazones, in particular rosiglitazone, troglitazone and pioglitazone, sulfonyl urea derivatives and metformin results not only in a beneficial, especially a **synergistic**, therapeutic effect, but also in additional benefits resulting from the combined treatment and further surprising beneficial effects compared to a. . .

SUMM . . . nateglinide or a pharmaceutically acceptable salt thereof and an antidiabetic thiazolidinedione derivative, results not only in a beneficial, especially a **synergistic**, therapeutic effect but also in additional benefits resulting from combined treatment such as a surprising prolongation of efficacy, a broader. . .

SUMM If taken simultaneously, this results not only in a further enhanced beneficial, especially a **synergistic**, therapeutic effect, but also in additional benefits resulting from the simultaneous treatment such as a surprising prolongation of efficacy, a. . .

SUMM These studies prove in particular the **synergism** of the claimed combinations, such as the combined preparations or pharmaceutical compositions, respectively. The beneficial effects on diseases and conditions. . .

SUMM . . . antidiabetic compound selected from the group consisting of glitazones, sulfonyl urea derivatives and metformin results in a beneficial, especially a **synergistic**, therapeutic effect, especially on type 2 diabetes, and also in additional benefits such as a decrease of diabetes-related mortality, a. . .

SUMM . . . thereof may vary within wide limits especially depending of the nature of the compounds selected. In order to obtain a **synergistic** effect of the components, preferably the ratio of nateglinde or a pharmaceutically acceptable salt thereof to the glitazone is between. . .

SUMM . . . in free or pharmaceutically acceptable salt form, simultaneously or sequentially in any order, in jointly therapeutically effective amounts, preferably in **synergistically** effective amounts, e.g. in daily dosages corresponding to the ratios described herein.

IT 557-04-0 657-24-9, Metformin 1115-70-4, Metformin hydrochloride 9003-39-8, Povidone 9004-10-8, Insulin, biological studies 64044-51-5, Lactose monohydrate 74811-65-7, Croscarmellose sodium 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 135062-02-1, Repaglinide
(pharmaceuticals contg. nateglinide or repaglinide for treating diabetes or conditions assocd. with diabetes)

L26 ANSWER 4 OF 30 USPATFULL on STN
AN 2003:106732 USPATFULL
TI Combinations comprising a beta-agonist and a further antidiabetic agent
IN Sanders Arch, Jonathan Robert, Welwyn Garden City, UNITED KINGDOM
PA SmithKline Beecham p.l.c. (non-U.S. corporation)
PI US 2003073644 A1 20030417
AI US 2002-243164 A1 20020913 (10)
RLI Continuation of Ser. No. US 2001-831651, filed on 11 Jul 2001, ABANDONED A 371 of International Ser. No. WO 1999-GB3755, filed on 11 Nov 1999, UNKNOWN
PRAI GB 1998-24789 19981111
GB 1998-24791 19981111
GB 1998-24790 19981111
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW 2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . aspect, the particularly beneficial effect on glycaemic control provided by the treatment of the invention is indicated to be a **synergistic** effect relative to the control expected from the effects of the individual active agents.
IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 339-43-5, Carbutamide 631-27-6, Glyclopyramide 657-24-9, Metformin 664-95-9, Glycyclamide 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol 74772-77-3, Ciglitazone 74772-77-3D, Ciglitazone, derivs. 80879-63-6, Emiglitate 83480-29-9, Voglibose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 97322-87-7D, Troglitazone, derivs. 109229-58-5, Englitazone 109229-58-5D, Englitazone, derivs. 111025-46-8, Pioglitazone 111025-46-8D, Pioglitazone, derivs. **122320-73-4 122320-73-4D**, derivs. 193759-90-9 193759-94-3 193759-96-5 193759-98-7
193760-02-0 193760-04-2 193760-06-4 193760-08-6 193760-13-3
193760-25-7 193760-28-0 193760-31-5 193760-41-7 193760-43-9
193760-55-3 193760-59-7 193760-63-3 193760-81-5 193760-89-3
193760-93-9 193761-11-4 193761-29-4 193761-31-8 193761-36-3
268727-70-4 268727-71-5 268727-72-6 268727-73-7 268727-74-8
268727-75-9 268727-76-0 268727-77-1 268727-78-2 268727-79-3
268727-80-6 268727-81-7 268727-82-8 268727-83-9 268727-84-0
268727-85-1 268727-86-2 268727-88-4 268727-89-5 268727-90-8
268727-91-9 268727-92-0 268727-93-1 268727-94-2 268727-95-3
268727-96-4 268727-97-5 268727-98-6 268727-99-7 268728-00-3
268728-01-4 268728-02-5 268728-03-6 268728-04-7 268728-05-8
268728-06-9 268728-07-0 268728-08-1 268728-09-2 268728-10-5
268728-11-6 268728-12-7 268728-13-8 268728-14-9 268728-15-0
268728-16-1 268728-17-2 268728-18-3 268728-19-4 268728-20-7
268728-21-8 268728-22-9 268728-23-0 268728-24-1 268728-25-2
268728-26-3 268728-27-4 268728-28-5 268728-29-6 268728-30-9
268728-31-0 268728-32-1 268728-33-2 268728-34-3 268728-35-4
268728-36-5 268728-37-6 268728-38-7 268728-39-8 268728-40-1
(.beta.-agonist-antidiabetic combination for treatment of diabetes mellitus and conditions assocd. with diabetes)

L26 ANSWER 5 OF 30 USPATFULL on STN
AN 2003:86880 USPATFULL
TI Drug comprising combination
IN Sugiyama, Yasuo, Kawanishi-shi,Hyogo, JAPAN
Odaka, Hiroyuki, Kobe-shi, Hyogo, JAPAN
Naruo, Ken-ichi, Sanda-shi,Hyogo, JAPAN
PI US 2003060488 A1 20030327
AI US 2002-203300 A1 20020809 (10)
WO 2001-JP880 20010208
PRAI JP 2000-38265 20000210
DT Utility
FS APPLICATION
LREP WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1215
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . vascular complications and hypoglycemia induction are less likely to be caused, which are harmful effects of insulin overdose,

because a **synergistic** effect can be afforded or the amount of insulin used is reduced as compared to that of the single administration. . .

IT 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 134523-00-5, Atorvastatin 145599-86-6, Cerivastatin 147098-20-2, ZD-4522 147511-69-1, Itavastatin
(TNF-.alpha. inhibitors contg. combination of insulin resistance-ameliorating agents with HMG-CoA reductase inhibitors)

L26 ANSWER 6 OF 30 USPATFULL on STN
AN 2003:30867 USPATFULL
TI Combined use of derivatives of GLP-1 analogs and PPAR ligands
IN Knudsen, Liselotte Bjerre, Valby, DENMARK
Wassermann, Karsten, Gentofte, DENMARK
Sturis, Jeppe, Vaerlose, DENMARK
Brand, Christian Lehn, Allerod, DENMARK
PI US 2003022816 A1 20030130
AI US 2001-949344 A1 20010907 (9)
RLI Continuation-in-part of Ser. No. US 2001-800541, filed on 7 Mar 2001, PENDING
DT Utility
FS APPLICATION
LREP Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405 Lexington Avenue, New York, NY, 10174-6401
CLMN Number of Claims: 62
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 855
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . of GLP-1 and thiazolidinedione for treatment of NIDDM. A side effect of thiazolidinedione was stated to be reduced and a **synergistic** effect of combining GLP-1 with thiazolidinedione has been alleged.
SUMM . . . and the stable derivative of a GLP-1 analog are administered in amounts and for a sufficient time to produce a **synergistic** effect.
SUMM [0024] **Synergistic** effect: A **synergistic** effect of two compounds is in terms of statistical analysis an effect which is greater than the additive effect which. . .
DETD [0027] It has been discovered that in the treatment of diabetes there is a **synergistic** effect of stable derivatives of GLP-1 analogs and non-thiazolidinedione PPAR ligands. Treatment of Zucker Diabetic Fatty (ZDF) rats with a. . . experimental results showed a significant interaction which demonstrate that combined treatment with non-thiazolidinedione PPAR ligands and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup..alpha.-hexadecanoyl)))-GLP-1(7-37) has profound **synergistic** effects on HbA.sub.1c and the 24-hour plasma glucose profile.
DETD [0028] A strong **synergistic** effect of two compounds permits the dosages of these compounds in the combined treatment to be below the optimal dosages. . .
DETD . . . GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in sufficient amount and for a sufficient time to produce a **synergistic** effect, preferably for at least 4 weeks.
DETD [0064] **Synergistic** effect of combining (-)-2-ethoxy-3-(4-(2-phenoxazin-10-yl-ethoxy)-phenyl)-propionic acid and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup..alpha.-hexadecanoyl)))-GLP-1(7-37) on glucose and HbA.sub.1c (glycosylated hemoglobin) in the male ZDF rat.
DETD . . . that four weeks combination treatment with (-)-2-ethoxy-3-(4-(2-

phenoxazin-10-yl-ethoxy)-phenyl)-propionic acid (1 mg/kg, once daily) and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup..alpha.-hexadecanoyl)))-GLP-1(7-37) (50 .mu.g/kg, twice daily) has **synergistic** (greater than additive) effects on HbA.sub.1c and 24-hour glucose profiles in overtly diabetic ZDF rats.

CLM What is claimed:

. . . a GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in amounts and for a sufficient time to produce a **synergistic** effect.

. . . a GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in amounts and for a sufficient time to produce a **synergistic** effect.

IT 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 199113-98-9, 5-[[4-(3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl)methoxy]phenylmethyl]thiazolidine-2,4-dione 204656-20-2 222834-30-2
(combined use of derivs. of GLP-1 analogs and PPAR ligands for treatment of diabetes and dyslipidemia)

L26 ANSWER 7 OF 30 USPATFULL on STN
AN 2003:24218 USPATFULL
TI Novel remedies with the use of beta 3 agonist
IN Ogawa, Kohei, Shizuoka, JAPAN
Umeno, Hiroshi, Shizuoka, JAPAN
PI US 2003018061 A1 20030123
AI US 2002-182375 A1 20020729 (10)
WO 2001-JP553 20010126
PRAI JP 2000-20733 20000128
DT Utility
FS APPLICATION
LREP YOUNG & THOMPSON, 745 SOUTH 23RD STREET 2ND FLOOR, ARLINGTON, VA, 22202
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0126] Therefore, the therapeutic agent used in combination of the present invention exhibited a strong **synergistic** effect in therapeutic effects for pollakiuria and incontinence of urine, and it was confirmed that it is useful as a. . .
DETD . . . act therein. By combined use of pravastatin and a .beta.3 agonist, which have different action mechanisms to each other, a **synergistic** decrease in the blood cholesterol level and level of triglyceride in blood can be acknowledged.
IT 56-03-1D, Biguanide, derivs. 59-67-6, Nicotinic acid, biological studies 637-07-0, Clofibrate 1508-65-2, Oxybutynin hydrochloride 9004-10-8, Insulin, biological studies 10238-21-8, Glibenclamide 41859-67-0, Bezafibrate 56180-94-0, Acarbose 60569-19-9, Propiverine 81093-37-0, Pravastatin 97322-87-7, Troglitazone 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 124937-51-5, Tolterodine 161600-01-7, MCC 555 170861-63-9, JTT 501 193760-08-6 213252-19-8, KRP 297 268727-76-0 268728-01-4 268728-06-9 268728-13-8 274687-78-4, GI 262570 333754-68-0 352194-77-5
(novel remedies with the use of .beta.3 agonists as antidiabetics and antilipidemics and for treatment of urination disorder)

L26 ANSWER 8 OF 30 USPATFULL on STN
AN 2002:330243 USPATFULL
TI Combined use of derivatives of GLP-1 analogs and PPAR ligands
IN Knudsen, Liselotte Bjerre, Valby, DENMARK

Wassermann, Karsten, Gentofte, DENMARK
Sturis, Jeppe, Vaerlose, DENMARK
Brand, Christian Lehn, Allerod, DENMARK

maleate

PI US 2002187926 A1 20021212
AI US 2001-951300 A1 20010913 (9)
RLI Continuation-in-part of Ser. No. US 2001-800541, filed on 7 Mar 2001, PENDING
DT Utility
FS APPLICATION
LREP Reza Green, Esq., Novo Nordisk of North America, Inc., Suite 6400, 405 Lexington Avenue, New York, NY, 10174-6401
CLMN Number of Claims: 74
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . of GLP-1 and thiazolidinedione for treatment of NIDDM. A side effect of thiazolidinedione was stated to be reduced and a **synergistic** effect of combining GLP-1 with thiazolidinedione has been alleged.

SUMM . . . and the stable derivative of a GLP-1 analog are administered in amounts and for a sufficient time to produce a **synergistic** effect.

SUMM [0023] **Synergistic** effect: A **synergistic** effect of two compounds is in terms of statistical analysis an effect which is greater than the additive effect which. . .

SUMM [0026] It has been discovered that in the treatment of diabetes there is a **synergistic** effect of stable derivatives of GLP-1 analogs and non-thiazolidinedione PPAR ligands. Treatment of Zucker Diabetic Fatty (ZDF) rats with a. . . experimental results showed a significant interaction which demonstrate that combined treatment with non-thiazolidinedione PPAR ligands and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup..alpha.-hexadecanoyl)))-GLP-1(7-37) has profound **synergistic** effects on HbA.sub.1c and the 24-hour plasma glucose profile.

SUMM [0027] A strong **synergistic** effect of two compounds permits the dosages of these compounds in the combined treatment to be below the optimal dosages. . .

SUMM . . . GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in sufficient amount and for a sufficient time to produce a **synergistic** effect, preferably for at least 4 weeks.

DETD [0062] **Synergistic** effect of combining (-)-2-ethoxy-3-(4-(2-phenoxazin-10-yl-ethoxy)-phenyl)-propionic acid and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup..alpha.-hexadecanoyl)))-GLP-1(7-37) on glucose and HbA.sub.1 (glycosylated hemoglobin) in the male ZDF rat.

DETD . . . four weeks combination treatment with (-)-2-ethoxy-3-(4-(2-phenoxazin-10-yl-ethoxy)-phenyl)-propionic acid (1 mg/kg, once daily) and Arg.sup.34, Lys.sup.26(N.sup..epsilon.-(.gamma.-Glu(N.sup.60 -hexadecanoyl)))-GLP-1(7-37) (50 .mu.g/kg, twice daily) has **synergistic** (greater than additive) effects on HbA.sub.1 and 24-hour glucose profiles in overtly diabetic ZDF rats.

CLM What is claimed is:

. . . a GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in amounts and for a sufficient time to produce a **synergistic** effect.

. . . a GLP-1 analog and the non-thiazolidinedione PPAR ligand are administered in amounts and for a sufficient time to produce a **synergistic** effect.

IT 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone

(insulin sensitizer; combined use of derivs. of GLP-1 analogs and PPAR ligands for treatment of diabetes and dyslipidemia)

L26 ANSWER 9 OF 30 USPATFULL on STN
AN 2002:259463 USPATFULL
TI Methods and compositions for the treatment of alopecia and other disorders of the pilosebaceous apparatus
IN Krajcik, Rozlyn A., Poughquag, NY, UNITED STATES
Orentreich, Norman, New York, NY, UNITED STATES
PA Orentreich Foundation for the Advancement of Science, Inc., New York, NY, UNITED STATES (U.S. corporation)
PI US 2002143039 A1 20021003
AI US 2002-73607 A1 20020211 (10)
RLI Continuation of Ser. No. WO 2001-US5653, filed on 23 Feb 2001, UNKNOWN
PRAI US 2000-184398P 20000223 (60)
DT Utility
FS APPLICATION
LREP AKIN, GUMP, STRAUSS, HAUER & FELD, L.L.P., ONE COMMERCE SQUARE, 2005 MARKET STREET, SUITE 2200, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 772
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . to more frequent (twice or thrice daily) ISIS dosing, may be expected, but this does not add to the inherent **synergism** of the therapies.
IT 52-01-7, Spironolactone 56-03-1D, Biguanide, derivs. 57-83-0, Progesterone, biological studies 102-02-3, Phenyl biguanide 427-51-0, Cyproterone acetate 643-12-9, D-Chiro-Inositol 976-71-6, Canrenone 1115-70-4 2295-31-0D, Thiazolidinedione, derivs. 13311-84-7, Flutamide 34461-22-8, Metformin pamoate 51481-61-9, Cimetidine 63612-50-0, Nilutamide 65277-42-1, Ketoconazole 73671-86-0, 4-MA 74772-77-3, Ciglitazone 90357-06-5, Bicalutamide 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 154992-24-2, RU-58841
(compns. contg. insulin-sensitivity increasing compds. for treatment of alopecia and other disorders of pilosebaceous app.)

L26 ANSWER 10 OF 30 USPATFULL on STN
AN 2002:251826 USPATFULL
TI Differentiating agents for the treatment of inflammatory intestinal diseases
IN Wu, Gary W., Ardmore, PA, UNITED STATES
PI US 2002137780 A1 20020926
AI US 2001-896984 A1 20010702 (9)
RLI Continuation-in-part of Ser. No. US 1999-457790, filed on 9 Dec 1999, PENDING Continuation-in-part of Ser. No. US 1999-256165, filed on 23 Feb 1999, ABANDONED Continuation-in-part of Ser. No. US 1995-413806, filed on 30 Mar 1995, PATENTED Continuation-in-part of Ser. No. US 1995-387116, filed on 13 Feb 1995, PATENTED
DT Utility
FS APPLICATION
LREP LICATLA & TYRRELL P.C., 66 E. MAIN STREET, MARLTON, NJ, 08053
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . conjunction with inhibitors of inflammatory mediators produced by immunocytes such as IL-1 receptor antagonist and cyclosporin, will result in a **synergistic** anti-inflammatory effect.

IT 122-79-2, Phenylacetate 137-40-6, Sodium propionate 156-54-7, Sodium butyrate 32511-63-0, 1,25-Dihydroxy vitamin D3 **122320-73-4**, Rosiglitazone
(differentiating agents for treatment of inflammatory intestinal diseases)

L26 ANSWER 11 OF 30 USPATFULL on STN
AN 2002:235080 USPATFULL
TI Peroxisome proliferator-acitvated receptor gamma ligand eluting medical device
IN Carlyle, Wenda, Petaluma, CA, UNITED STATES
Cheng, Peiwen, Santa Rosa, CA, UNITED STATES
Cafferata, Robert L., Santa Rosa, CA, UNITED STATES
PI US 2002127263 A1 20020912
AI US 2002-85539 A1 20020226 (10)
PRAI US 2001-271898P 20010227 (60)
DT Utility
FS APPLICATION
LREP Christine Aceves, Medtronic AVE, 3576 Unocal Place, Santa Rosa, CA, 95403
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 947
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . compound coated stent can be combined with the local delivery of the same or another anti-restenotic compound to achieve a **synergistic** effect at the medical device placement site. This is particularly beneficial in that non-toxic therapeutic levels of both the thiazolidinediones and other anti-restenotic therapeutic can be combined to achieve dose specific **synergism**.
DETD [0028] The thiazolidinediones and other PPAR.gamma. agonists of the present invention are delivered, alone or in combination with **synergistic** and/or additive therapeutic agents, directly to the affected area using medical devices. Potentially **synergistic** and/or additive therapeutic agents may include drugs that impact a different aspect of the restenosis process such as antiplatelet, antimigratory. . . but through a different mechanism than by binding to the PPAR.gamma. receptor. For example, and not intended as a limitation, **synergistic** combination considered to within the scope of the present invention include at least one thiazolidinedion and an antisense anti-c-myc oligonucleotide,. . .
IT 2295-31-0D, Thiazolidinedione, derivs. 74772-77-3, Ciglitazone 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone 141200-24-0, Darglitazone
(medical devices for site-specific delivery of PPAR.gamma. receptor agonists for restenosis inhibition)

L26 ANSWER 12 OF 30 USPATFULL on STN
AN 2002:209569 USPATFULL
TI Use of RAR antagonists as modulators of hormone mediated processes
IN Evans, Ronald M., La Jolla, CA, United States
Tontonoz, Peter J., Los Angeles, CA, United States
Nagy, Laszlo, San Diego, CA, United States
PA The Salk Institute for Biological Studies, La Jolla, CA, United States (U.S. corporation)
PI US 6436993 B1 20020820
US 2002137794 A1 20020926
AI US 1999-352816 19990713 (9)
DT Utility
FS GRANTED

EXNAM Primary Examiner: Jarvis, William; Assistant Examiner: Kim, Vickie
LREP Reiter, Stephen E., Foley & Lardner
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 936
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . not respond to RXR ligands unless ligands for RAR are already present, in which case they yield an additive or **synergistic** response (Apfel et al., J Biol Chem. 270(51):30765-72.(1995); Chen et al. PNAS 93:7567-7571 (1996)). Other non-permissive heterodimers include TR:RXR and. . .
CLM What is claimed is:
1. A **synergistic** composition for modulating hormone mediated process(es) comprising an effective amount of: at least one agonist for a member of the. . .
IT 65-85-0D, Benzoic acid, derivs., biological studies 71-43-2D, Benzene, derivs., biological studies 74-86-2D, Acetylene, aryl derivs. 91-20-3D, Naphthalene, derivs., biological studies 119-64-2D, Tetrahydronaphthalene, derivs. 120-12-7D, Anthracene, derivs., biological studies 132-64-9D, Dibenzofuran, derivs. 254-04-6D, 2H-1-Benzopyran, benzo derivs. 254-04-6D, Benzopyran, derivs. 254-37-5D, 2H-1-Benzothiopyran, derivs. 260-42-4D, 2H-Naphtho[2,3-b]pyran, derivs. 260-49-1D, 2H-Naphtho[2,3-b]thiopyran, derivs. 281-23-2D, Adamantane, biarom. derivs. 447-53-0D, derivs. 504-78-9D, Thiazolidine, derivs. 582-80-9D, derivs. 612-18-0D, 1,2-Dihydroquinoline, derivs. 780-68-7D, 1-Phenyladamantane, derivs. 12688-68-5D, Diazepine, derivs. 14721-66-5, Phytanic acid 16872-09-6D, 1,2-Dicarbadodecaborane(12), derivs. 18104-45-5, 13-HODE 25448-04-8D, Tetrahydroquinoline, derivs. 29828-28-2D, Dihydronaphthalene, derivs. 50892-23-4, WY14643 87893-55-8, 15-Deoxy-.DELTA.12,14-prostaglandin J2 97322-87-7, Troglitazone 98524-19-7 **122320-73-4**, Rosiglitazone 144092-31-9, Ro41-5253 158301-69-0, ER27191 158302-04-6 164108-15-0, BMS411 170355-78-9, CD2665 171746-21-7, AGN193109 188645-44-5, LE540 196808-24-9 196808-45-4 196808-60-3 196809-33-3 219653-36-8 321126-06-1 321126-07-2D, derivs. 321126-08-3 321557-86-2
(RAR antagonists as modulators of hormone-mediated processes)

L26 ANSWER 13 OF 30 USPATFULL on STN
AN 2002:198695 USPATFULL
TI PAX8-PPARgamma nucleic acid molecules and polypeptides and uses thereof
IN Fletcher, Jonathan A., Brookline, MA, UNITED STATES
Kroll, Todd G., Newton Highlands, MA, UNITED STATES
PI US 2002106796 A1 20020808
AI US 2001-765111 A1 20010118 (9)
PRAI US 2000-177109P 20000120 (60)
US 2000-225079P 20000814 (60)
DT Utility
FS APPLICATION
LREP Elizabeth R. Plumer, c/o Wolf, Greenfield & Sacks, P.C., Federal Reserve Plaza, 600 Atlantic Avenue, Boston, MA, 02210-2211
CLMN Number of Claims: 62
ECL Exemplary Claim: 1
DRWN 6 Drawing Page(s)
LN.CNT 3762
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . in time with the administration of the therapeutic agent so that the two compounds may exert an additive or even **synergistic** effect, (e.g., reducing a tumor mass).
IT 74772-68-2 74772-77-3 87858-57-9 97322-87-7 103787-97-9 109229-58-5, Englitazone 111025-46-8, pioglitazone 118384-10-4

119670-18-7 122320-46-1 **122320-73-4** 125734-02-3
127810-37-1 132646-45-8 134539-13-2 134868-21-6 141109-81-1
141200-24-0 142649-73-8 143811-62-5 168190-63-4 168190-68-9
168190-78-1 168190-79-2 168190-89-4 168190-91-8 168190-93-0
168191-00-2 350685-90-4D, alkyl derivs.
(DNA encoding human chimeric oncoprotein PAX8-PPAR.gamma. found in thyroid follicular carcinomas)

L26 ANSWER 14 OF 30 USPATFULL on STN
AN 2002:99423 USPATFULL
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and alpha glucocidase inhibitor
IN Buckingham, Robin Edwin, Welwyn Garden City, UNITED KINGDOM
Smith, Stephen Alistair, Bramfield, UNITED KINGDOM
PA SmithKline Beecham plc (non-U.S. corporation)
PI US 2002052324 A1 20020502
AI US 2001-989572 A1 20011120 (9)
RLI Continuation of Ser. No. US 1999-445908, filed on 15 Dec 1999, PENDING A 371 of International Ser. No. WO 1998-GB2112, filed on 16 Jul 1998, UNKNOWN
PRAI GB 1997-15298 19970718
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 487
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0046] The particularly beneficial effect on glycaemic control provided by the treatment of the invention is indicated to be a **synergistic** effect relative to the control expected for the sum of the effects of the individual active agents.
IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 631-27-6, Glyclopyramide 664-95-9, Glycyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol 74772-77-3, Ciglitazone 80879-63-6, Emiglitate 93479-97-1, Glimepiride 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4** 135062-02-1, Repaglinide 155141-29-0
(thiazolidinedione, insulin secretagogue, and .alpha.-glucosidase inhibitor for diabetes treatment)

L26 ANSWER 15 OF 30 USPATFULL on STN
AN 2002:88529 USPATFULL
TI Metforimin-containing compositions for the treatment of diabetes
IN Fine, Stuart A., Northbrook, IL, United States
Kinsella, Kevin J., La Jolla, CA, United States
PA Akesis Pharmaceuticals, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 6376549 B1 20020423
AI US 1998-156102 19980917 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Criares, Theodore J.
LREP Foley, Hoag & Eliot LLP
CLMN Number of Claims: 40
ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1429
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat diabetes.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat diabetes mellitus.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat elevated HbA1c levels in a subject having elevated HbA1c levels.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat daily blood glucose fluctuations in a subject susceptible to daily blood glucose fluctuations.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** improve the ability of a subject to metabolize glucose.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** reduce blood sugar levels in a subject susceptible to abnormal fluctuations in blood sugar levels.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat hyperglycemia in a subject having hyperglycemia.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** treat insulin resistance syndrome in a subject having insulin resistance syndrome.

. . . acceptable salts thereof; and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components **synergistically** reduce the dosage of anti-diabetic medication needed for treatment of a diabetic subject.

. . . and one or more of a bioavailable source of vanadium and pharmaceutically acceptable salts thereof; which components of said composition **synergistically** reduce the effective amount of insulin needed.

IT 50-78-2, Aspirin 64-77-7, Tolbutamide 65-85-0D, Benzoic acid, derivs., biological studies 94-20-2, Chlorpropamide 657-24-9, Metformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1406-18-4, Vitamin E 2295-31-0D, Thiazolidinedione, derivs. 7439-95-4, Magnesium, biological studies 7440-47-3, Chromium, biological studies 7440-62-2, Vanadium, biological studies 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14639-25-9 14639-25-9D, oligomeric 21187-98-4, Gliclazide 27774-13-6 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 93479-97-1, Glimepiride 97322-87-7, Troglitazone 111025-46-8, Pioglitazone **122320-73-4,**

Rosiglitazone 135062-02-1, Repaglinide
(compns. for treatment of glucose metab. disorders)

L26 ANSWER 16 OF 30 USPATFULL on STN
AN 2002:67275 USPATFULL
TI Combination therapeutic compositions and method of use
IN Jaen, Juan C., Burlingame, CA, UNITED STATES
Chen, Jin-Long, Foster City, CA, UNITED STATES
PI US 2002037928 A1 20020328
AI US 2001-847887 A1 20010502 (9)
PRAI US 2000-201613P 20000503 (60)
DT Utility
FS APPLICATION
LREP TOWNSEND AND TOWNSEND AND CREW, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1692
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . approximately equal to the sum of the effects of each drug alone), but in other cases the effect can be **synergistic** (the efficacy of the combination is greater than the sum of the effects of each drug given alone). In real medical practice, it is often quite difficult to determine if drug combinations are additive or **synergistic**.
SUMM [0053] The terms "**synergistic** effective amount" refers to a combined amount of both a compound of Formula I and an antidiabetic agent that is effective to cause a **synergistic** effect. Synergy is a biological phenomenon in which the effectiveness of two active components in a mixture is more than. . . In certain aspects, the effectiveness of the combination therapy of a compound of Formula I and an antidiabetic agent is **synergistic**. Thus, **synergism** is a result, or function, that is more than the sum of the results, or functions of individual elements.
IT 50-18-0, Cyclophosphamide 50-78-2, Aspirin 52-53-9, Verapamil 53-03-2, Prednisone 53-86-1, Indomethacin 55-63-0, Nitroglycerin 56-03-1D, Biguanide, derivs. 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 64-77-7, Tolbutamide 64-86-8, Colchicine 86-54-4, Hydralazine 94-20-2, Chlorpropamide 114-07-8, Erythromycin 114-86-3, Phenformin 124-94-7, Triamcinolone 154-93-8, Carmustine 300-62-9, Amphetamine 315-30-0, Allopurinol 339-44-6, Glymidine 451-71-8, Glyhexamide 518-28-5, Podophyllotoxin 525-66-6, Propranolol 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1406-18-4, Vitamin E 3149-00-6, Phenbutamide 4205-90-7, Clonidine 4759-48-2, Isotretinoin 5581-42-0, Glyparamide 5588-38-5, Tolpyrramide 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 10540-29-1, Tamoxifen 13010-20-3D, Nitrosourea, metal derivs. 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 15663-27-1, Cisplatin 19216-56-9, Prazocine 21187-98-4, Gliclazide 23214-92-8, Doxorubicin 24455-58-1, Glicetanile 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 33069-62-4, Paclitaxel 33342-05-1, Gliquidone 33419-42-0, Etoposide 35273-88-2, Gliflumide 42399-41-7, Diltiazem 45086-03-1, Etoformin 50925-79-6, Colestipol 51876-98-3, Gliamilide 56180-94-0, Acarbose 59865-13-3, Cyclosporine 62571-86-2, Captopril 72432-03-2, Miglitol 74772-77-3, Ciglitazone 79902-63-9, Simvastatin 80879-63-6, Emiglitate 83480-29-9, Voglibose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 103787-97-9, BM 131246 103788-05-2, AD-5075 104343-33-1, MDL-25637 104987-11-3, FK-506 106650-56-0, Sibutramine 109229-58-5, Englitazone 111025-46-8, Pioglitazone 114798-26-4, Losartan 120014-06-4,

Donepezil **122320-73-4**, Rosiglitazone 127214-23-7, Camiglibose 141200-24-0, Darglitazone 170861-63-9, JTT-501 199914-96-0 371968-35-3D, derivs.
(benzene compds. in combination therapy for diabetes and diabetes-related disorders)

L26 ANSWER 17 OF 30 USPATFULL on STN
AN 2002:27439 USPATFULL
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and diguanide
IN Buckingham, Robin Edwin, Wel Wyn Garden City, UNITED KINGDOM
Smith, Stephen Alistair, Bramfield, UNITED KINGDOM
PA SmithKline Beecham p.l.c. (non-U.S. corporation)
PI US 2002016287 A1 20020207
AI US 2001-939470 A1 20010824 (9)
RLI Continuation of Ser. No. US 1999-446039, filed on 15 Dec 1999, PENDING A 371 of International Ser. No. WO 1999-GB9802110, filed on 28 Jan 1999, UNKNOWN
PRAI GB 1997-15295 19970718
DT Utility
FS APPLICATION
LREP GLAXOSMITHKLINE, Corporate Intellectual Property - UW2220, P.O. Box 1539, King of Prussia, PA, 19406-0939
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 479
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD [0046] The particularly beneficial effect on glycaemic control provided by the treatment of the invention is indicated to be a **synergistic** effect relative to the control expected for the sum of the effects of the individual active agents.
IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 339-43-5, Carbutamide 631-27-6, Glyclopyramide 657-24-9, Metformin 664-95-9, Glycyclamide 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 74772-77-3, Ciglitazone 93479-97-1, Glimepiride 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4** 135062-02-1, Repaglinide 155141-29-0
(thiazolidinedione, insulin secretagogue, and biguanide for diabetes treatment)

L26 ANSWER 18 OF 30 USPATFULL on STN
AN 2002:22432 USPATFULL
TI **Synergistic** effect of a sulfonylurea and/or non-sulfonylurea Kchannel blocker, and a phosphodiesterase 3 type inhibitor
IN Fryburg, David A., East Lyme, CT, UNITED STATES
Parker, Janice C., Ledyard, CT, UNITED STATES
PI US 2002013268 A1 20020131
AI US 2001-829874 A1 20010410 (9)
PRAI US 2000-196728P 20000413 (60)
DT Utility
FS APPLICATION
LREP Gregg C. Benson, Pfizer Inc., Patent Department, MS 4159, Eastern Point Road, Groton, CT, 06340
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 1475

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI **Synergistic** effect of a sulfonylurea and/or non-sulfonylurea Kchannel blocker, and a phosphodiesterase 3 type inhibitor

AB . . . Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance using a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . the methods comprising the step of administering to a patient having or at risk of having non-insulin dependent diabetes a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . resistance, the methods comprising the step of administering to a patient having or at risk of having insulin resistance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . X, the methods comprising the step of administering to a patient having or at risk of having Syndrome X a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . having or at risk of having diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, or cataracts a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . treating hyperglycemia, the methods comprising the step of administering to a patient having or at risk of having hyperglycemia a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

SUMM . . . the methods comprising the step of administering to a patient having or at risk of having impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

DRWD [0062] FIG. 1 is an isobologram that shows the **synergistic** effect of combinations of milrinone and glyburide on insulin secretion.

DETD . . . Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

DETD [0067] The phrase "**synergistic** amount" means that the therapeutic effect of a sulfonylurea and/or non-sulfonylurea K.sup.+ ATP channel blocker, when administered in combination with. . .

DETD . . . K.sup.+ ATP channel blockers, and CAMP phosphodiesterase type 3 inhibitors of the present invention are administered to a patient in **synergistic** amounts. It has been surprisingly and unexpectedly discovered that administration of a combination of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+. . .

DETD . . . ATP channel blockers, and cAMP phosphodiesterase type 3 inhibitors of the present invention can be administered to a patient at **synergistic** dosage levels in the range of about 0.1 to about 7,000 mg per day. A preferred dosage range is about. . .

DETD [0095] Suitable **synergistic** dosage ranges can be correlated with desired plasma concentrations. For example, an effective plasma concentration of a cAMP phosphodiesterase type. . .

DETD . . . or non-orally, for example by injection. An amount of a compound or combination of compounds is administered such that a **synergistic** dose is received, generally a daily dose which, when administered orally to an animal is usually between 0.01 and 100. . .

DETD . . . Alternatively, such concentrated supplements may be added directly to the feed to produce a nutritionally balanced, finished feed containing a **synergistic** amount of the compounds according to the present invention. The mixtures are thoroughly blended by standard procedures, such as in. . .

DETD . . . can be treated by administering to a patient having or at risk of having one of the above-mentioned diseases a **synergistic** amount of: 1) a sulfonylurea and/or a non-sulfonylurea K.sup.+ ATP channel blocker; and 2) a cAMP phosphodiesterase type 3 inhibitor.. . . can be treated by administering to a patient having or at risk of having one of the above-mentioned diseases a **synergistic** amount a sulfonylurea and/or a non-sulfonylurea K.sup.+ ATP channel blocker, and a cAMP phosphodiesterase type 3 inhibitor and another agent. . .

DETD . . . data from the experiments. The plot in FIG. 1 is called an isobologram. Isobologorams are used in the study of **synergism** and are well known to those skilled in the art. If only an additive effect exists, the contour line would be a straight line connecting points C and D. **Synergism** exists if the actual contour is below the straight line.

DETD [0183] The magnitude of the **synergistic** effect is measured by how far the contour line is from the straight line. The line representing a fixed ratio. . . the additive straight line at point B. For a given ratio of the two drugs, we assess the magnitude of **synergistic** effect by a dose reduction factor r defined as: ##EQU1##

DETD . . . same level of response achieved by one unit of either drug individually. So if r is smaller than 1, then **synergism** exists. The smaller the r, the stronger the **synergistic** effect. It is possible to mathematically determine the ratio that produced the biggest **synergistic** effect and the dose reduction factor r associated with the ratio. We found that the ratio is glyburide/milrinone=2.4, and the. . . corresponding to one unit of either glyburide or milrinone alone. FIG. 1 shows that for a wide range of ratios **synergism** exists.

DETD . . . and standard deviation sd(r). This probability is the p-value. If the p-value is less than 0.05, we conclude that the **synergistic** effect is statistically significant. Table 1 lists the dose the associated p-value for each of the selected ratios of the two or each of the selected ratios, the **synergistic** effect is significant.

TABLE 1

Summary of Statistical Analysis Results

Glyburide/Milrinone	r	sd(r)	p-value

0.003	0.873	0.0236	3.45E-08
0.01	0.741	0.0358. . .	

DETD . . . From the statistical analysis, we conclude that over a wide range of ratios of combinations of the two drugs, the **synergistic** effect is statistically significant. We also found that the ratio of the two drugs that produced the maximum **synergistic** effect is glyburide/milrinone=2.4. With this ratio, only 0.259 of one unit of the combined amount of glyburide and milrinone was. . .

CLM What is claimed is:

. . . the method comprising the step of administering to a patient having or at risk of having non-insulin dependent diabetes a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

. . . resistance, the method comprising the step of administering to a patient having or at risk of having insulin resistance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

. . . X, the method comprising the step of administering to a patient having or at risk of having Syndrome X a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

. . . having or at risk of having diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, or cataracts a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

. . . treating hyperglycemia, the method comprising the step of administering to a patient having or at risk of having hyperglycemia a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

. . . the method comprising the step of administering to a patient having or at risk of having impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel. . .

IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 458-24-2, Fenfluramine 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 2295-31-0D, Thiazolidinedione, derivs. 7440-62-2D, Vanadium, complexes 9004-10-8D, Insulin, analogs 10238-21-8, Glyburide 21187-98-4, Gliclazide 23602-78-0, Benfluorex 28299-33-4D, Imidazoline, derivs. 29094-61-9, Glipizide 37353-31-4, Vanadate 51037-30-0, Acipimox 56180-94-0, Acarbose 60719-84-8, Amrinone 66529-17-7, Midaglizole 68550-75-4, Cilostamide 72432-03-2, Miglitol 73384-60-8 73963-72-1, Cilostazol 74150-27-9, Pimobendan 74772-77-3, Ciglitazone 75358-37-1, Linogliride 77671-31-9, Enoximone 78415-72-2, Milrinone 79944-58-4, Idazoxan 80879-63-6, Emiglitate 81840-15-5, Vesnarinone 83480-29-9, Voglibose 84243-58-3, Imazodan 86615-96-5, BRL 35135 88431-47-4, Clomoxir 89197-32-0, Efaroxan 90505-66-1, Ro 16-8714 90730-96-4, BRL 37344 93479-97-1, Glimepiride 94192-59-3, Lixazinone 97322-87-7, Troglitazone 100510-33-6, Adibendan 100643-96-7, Indolidan 102669-89-6, Saterinone 104343-33-1, MDL-25637 105182-45-4, Fluparoxan 105816-04-4, Nateglinide 106612-94-6, Insulinotropin (human) 107444-51-9 109229-58-5, Englitazone 110605-64-6, Isaglidole 111025-46-8, Pioglitazone 112018-01-6, Bemoradan 115344-47-3, Siguazodan **122320-73-4**, Rosiglitazone

122575-28-4, Naglivan 122830-14-2, Deriglidole 124083-20-1, Etomoxir
127214-23-7, Camiglibose 129689-30-1, ICI D7114 130714-47-5, WAG 994
133107-64-9 135062-02-1, Repaglinide 138908-40-4, CL316243
141200-24-0, Darglitazone 187887-46-3, Symlin 335149-21-8, AC2993
(sulfonylurea and/or non-sulfonylurea K+ ATP channel blocker and phosphodiesterase 3 type inhibitor synergism for treatment of non-insulin-dependent diabetes or other conditions)

L26 ANSWER 19 OF 30 USPATFULL on STN
AN 2002:12568 USPATFULL
TI METHODS AND PHARMACEUTICAL COMPOSITIONS FOR INHIBITING TUMOR CELL GROWTH
IN SPIEGELMAN, BRUCE M., WABAN, MA, UNITED STATES
ALTIOK, SONER, BOSTON, MA, UNITED STATES
MUELLER, ELISABETTA, BOSTON, MA, UNITED STATES
SARRAF, PASHA, BOSTON, MA, UNITED STATES
TONTONOZ, PETER, SAN DIEGO, CA, UNITED STATES
PA Dana-Farber Cancer Institute (U.S. corporation)
PI US 2002006950 A1 20020117
US 6552055 B2 20030422
AI US 1997-923346 A1 19970904 (8)
RLI Continuation of Ser. No. US 1996-766553, filed on 11 Dec 1996, ABANDONED
DT Utility
FS APPLICATION
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 2290
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . or which lack specficity for the treated cells, may be given in smaller doses due to an additive, and sometimes **synergistic** effect with the PPAR.gamma. agonist.
IT 74772-77-3, Ciglitazone 87893-55-8 97322-87-7, Troglitazone
109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**
, BRL 49653 167869-21-8, PD 98059 197730-94-2, LG 268 209264-01-7,
PD 147275
(thiazolidinedione PPAR.gamma. receptor agonists and compns. for inhibiting tumor cell growth)

L26 ANSWER 20 OF 30 USPATFULL on STN
AN 2002:12560 USPATFULL
TI Methods of treating liver disorders and disorders associated with liver function
IN Davis, Roger A., Solana Beach, CA, UNITED STATES
PI US 2002006942 A1 20020117
AI US 2001-792631 A1 20010223 (9)
PRAI US 2000-184592P 20000224 (60)
US 2000-187321P 20000306 (60)
DT Utility
FS APPLICATION
LREP Robert M. Bedgood, PILLSBURY WINTHROP LLP, 50 Freemont Street, San Francisco, CA, 94105
CLMN Number of Claims: 50
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . other drugs, therapeutic agents and herbal medicines. Such additional drugs, therapeutic agents and herbal medicines can provide an additive or **synergistic** effect when used in combination with a PPAR.gamma. agonist or antagonist.
IT 74772-77-3, Ciglitazone 97322-87-7, Troglitazone 103788-05-2, AD 5075

109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**
, BRL 49653 141200-24-0, Darglitazone 357434-86-7, Fluoroglitazone
(PPAR.gamma. agonist treatment of liver disorders by ameliorating inflammatory conditions produced by cytokines)

L26 ANSWER 21 OF 30 USPATFULL on STN
AN 2001:194440 USPATFULL
TI Method of inhibiting angiogenesis
IN Gerritsen, Mary E., San Mateo, CA, United States
Xin, Xiaohua E., San Francisco, CA, United States
PA Genentech, Inc. (U.S. corporation)
PI US 2001036955 A1 20011101
AI US 2001-865859 A1 20010525 (9)
RLI Continuation of Ser. No. US 1999-443010, filed on 17 Nov 1999, ABANDONED
PRAI US 1999-116530P 19990120 (60)
US 1998-109328P 19981120 (60)
DT Utility
FS APPLICATION
LREP BRINKS HOFER GILSON & LIONE, P.O. BOX 10395, CHICAGO, IL, 60610
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 2090
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . receptors (RXR) (Spiegelman, B. (1998) Diabetes 47:507-514). Specific ligands for the PPAR and RXR receptors have been shown to act **synergistically** to inhibit cancer cell growth (Elstner, E. et al., (1998) Proc. Natl. Acad. Sci. USA 95:8806-8811) and adipocyte differentiation (Spiegelrnan,. . .
DRWD [0032] FIG. 3C shows **synergistic** inhibition of tube formation by the combination of PPAR gamma and RXR specific ligands. Data are expressed as the percent. . .
DRWD [0047] A "**synergistic** effect" or a "**synergistic** manner" is an effect which is achieved by administering two compounds that is greater than the effect of either of. . .
DRWD . . . angiogenesis is inhibited by the administration of a PPAR gamma ligand/agonist and a retinoic acid (RXR) receptor ligand/agonist in a **synergistic** manner. In the inhibition of endothelial tube formation assay described above, administration of both types of compounds **synergistically** inhibits tube formation and angiogenesis to a greater degree than the inhibition caused by either compound alone. The compounds may. . .
DETD [0263] **Synergistic** inhibition of tube formation by HUVEC using 15d-PGJ.sub.2 and 9-cis-retinoic acid was demonstrated as follows. 9-Cis-retinoic acid is known to. . .
IT 13345-50-1, PGA2 13345-51-2, PGB1 13367-85-6, PGB2 14152-28-4, PGA1 17968-82-0, PGD1 41598-07-6, PGD2 60203-57-8, PGJ2 74772-77-3, Ciglitazone 87858-57-9 87893-54-7, .DELTA.12-PGJ2 87893-55-8, 15-Deoxy-.DELTA.12,14-PGJ2 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone 118384-10-4 119670-18-7 122320-46-1 **122320-73-4**, BRL 49653 125734-02-3 127810-37-1 132646-45-8 134539-13-2 134868-21-6 141109-81-1 141200-24-0 142649-73-8 143811-62-5 271263-69-5 271263-70-8
(PPAR.gamma. ligand/agonist for inhibiting angiogenesis and treating tumor growth)

L26 ANSWER 22 OF 30 USPATFULL on STN
AN 2001:158318 USPATFULL
TI Method and composition for the treatment of diabetes
IN Rieveley, Robert B., 4102 Yuculta Crescent, Vancouver, British Columbia, Canada V6N 3R5
PI US 6291495 B1 20010918

AI US 2000-608272 20000630 (9)
RLI Division of Ser. No. US 1997-804903, filed on 24 Feb 1997, now patented, Pat. No. US 6153632
DT Utility
FS GRANTED
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Oyen Wiggs Green & Mutala
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . efficiency that she experienced a hypoglycaemic condition. It appeared clear that there was a startling effect, and indeed perhaps a **synergistic** effect, created between the combination of insulin and the V-411 insulin sensitizer. Thus, much smaller dosages of insulin could have. . .
DETD . . . degradation effects of the gastric juices of the stomach and enzymatic action of the gut. Because of the strong or **synergistic** effect involving the combination of insulin and the insulin sensitizer, it follows that the inclusion of an insulin sensitizer in. . .
IT 56-03-1, Biguanide 98-98-6D, Picolinic acid, chromium derivs. 97322-87-7, Troglitazone 112529-15-4, Pioglitazone hydrochloride **122320-73-4**, BRL-49653 153559-49-0, LGD 1069 153559-76-3, ALRT 268 309956-37-4, MC 555
(diabetes mellitus treatment compns. contg. insulin sensitizers and antidiabetic agents)

L26 ANSWER 23 OF 30 USPATFULL on STN
AN 2001:82522 USPATFULL
TI Methods and pharmaceutical compositions for inhibiting tumor cell growth
IN Spiegelman, Bruce M., Waban, MA, United States
Altiok, Soner, Cambridge, MA, United States
Mueller, Elisabetta, Boston, MA, United States
Sarraf, Pasha, Boston, MA, United States
Tontonoz, Peter, San Diego, CA, United States
PA Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)
PI US 6242196 B1 20010605
WO 9825598 19980618
AI US 1999-319769 19990917 (9)
WO 1997-US22879 19971211
19990917 PCT 371 date
19990917 PCT 102(e) date
DT Utility
FS Granted
EXNAM Primary Examiner: Leary, Louise N.
LREP Lahive & Cockfield, LLP, Mandragouras, Amy E., Smith, DeAnn F.
CLMN Number of Claims: 35
ECL Exemplary Claim: 1
DRWN 36 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 2761
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . or which lack specificity for the treated cells, may be given in smaller doses due to an additive, and sometimes **synergistic** effect with the PPAR.gamma. agonist.
DETD . . . also limit the effectiveness of activation of this receptor with synthetic compounds. Studies with the 21MT cell line show a **synergistic** effect of troglitazone with a MAP kinase inhibitor strongly suggest that this protein kinase can regulate PPAR.gamma. function in these. . .

IT 74772-77-3, Ciglitazone 87893-55-8 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**, BRL 49653 167869-21-8, PD 98059 197730-94-2, LG 268 209264-01-7, PD 147275
(thiazolidinedione PPAR.gamma. receptor agonists and compns. for inhibiting tumor cell growth)

L26 ANSWER 24 OF 30 USPATFULL on STN
AN 2000:168044 USPATFULL
TI Treatment of arteriosclerosis and xanthoma
IN Tsujita, Yoshio, Tokyo, Japan
Horikoshi, Hiroyoshi, Tokyo, Japan
Shiomi, Masashi, Kobe, Japan
Ito, Takashi, Kobe, Japan
PA Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI US 6159997 20001212
AI US 1998-61446 19980416 (9)
RLI Division of Ser. No. US 1996-676090, filed on 2 Jul 1996, now patented, Pat. No. US 5798375
PRAI JP 1995-167291 19950703
DT Utility
FS Granted
EXNAM Primary Examiner: Criares, Theodore J.
LREP Frishauf, Holtz, Goodman, Langer & Chick, P.C.
CLMN Number of Claims: 210
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1910
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . more insulin sensitizers (for example troglitazone, pioglitazone, englitazone, BRL-49653, 5-(4-{2-[1-(4-2'-pyridylphenyl)ethylideneaminooxy]ethoxy}benzyl)thiazolidine-2,4-dione, 5-{4-(5-methoxy-3-methylimidazo[5,4-b]pyridin-2-ylmethoxy)benzyl}thiazolidine-2,4-dione or its hydrochloride, 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione, 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and 5-[4-(5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione) exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the. . .
SUMM . . . the application of a combination of one or more HMG-CoA reductase inhibitors with one or more insulin sensitizers exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the. . .
SUMM It is a further, and more specific object of the invention to provide such a combination exhibiting a **synergistic** effect.
SUMM . . . consisting of insulin sensitizers, said first and second agents being administered together or within such a period as to act **synergistically** together.
SUMM At present, the experimental evidence seems to us to suggest that the **synergistic** effect arises from an interaction between the modes of action of the two classes of compounds, the HMG-CoA reductase inhibitors. . .
SUMM . . . insulin resistance-improving agents. According to the invention, a combination of the HMG-CoA reductase inhibitor and the insulin sensitizer exhibits a **synergistic** effect in comparison with the application of the respective components alone, as shown below. Interestingly, such **synergism** appears to occur even if the compounds of the two classes do not always exist simultaneously in the body. That is, the **synergistic** effect may be observed even

when the concentration of one of the compounds of the two classes in the blood. . . from the previous administration of the other compound, and the effects of the two compounds operate together in a favourable **synergistic** manner. It is, of course, obvious that it may well be convenient to administer the two compounds simultaneously in clinical. . . separately in the form of single doses. As described above, since the compounds of the two classes exhibit together a **synergistic** effect, they may be administered almost simultaneously or at suitable intervals. The maximum interval acceptable for administering the compounds of the two classes in order to achieve the **synergistic** effect of the present invention may be confirmed by clinical practice or by experiments using animals.

SUMM . . . their original uses, that is as antihyperlipidemic and antidiabetic agents. Their doses are further lowered to some extent by the **synergistic** effect due to the combination of the compounds of the two classes. For example, where pravastatin and troglitazone are used. . .

DETD The present invention is further illustrated by the following Examples, which demonstrate the enhanced activity achieved by the **synergistic** combination of the present invention. In addition, the subsequent Formulations illustrate the pharmaceutical formulations which may be prepared and the. . .

DETD . . . (which received a combination of both agents) and group B (which received pravastatin alone). In contrast, there was observed clear **synergism** in the percent lesion area ratio (lesion area/total artery area in %) by comparing Group D (combination treatment) with Groups B and C (single agent treatment) as shown above. **Synergism** was observed in preventing coronary stenosis in respect of the left anterior descending artery, the left circumflex artery and the right coronary artery. Development of xanthoma on the digital joints was entirely prevented in Group D, thus demonstrating clear **synergism**.

DETD . . . reductase inhibitor and an insulin sensitizer with the groups administered the active agent alone, the combination of both active agents **synergistically** prevented progression of the arteriosclerosis, particularly of the thoracic aorta. These results could not be imagined from the state of. . .

DETD . . . results are that the two combinations of pravastatin, a HMG-CoA reductase inhibitor, and one of the thiazolidinedione insulin sensitizers exhibit **synergistic** effects on the treatment of atherosclerosis and on the occurrence of xanthoma.

DETD **Synergism** of HMG CoA reductase inhibitors and thiazolidinedione insulin sensitizers were examined on the regression of established atherosclerotic lesions in the. . .

DETD . . . showed no or little reduction of the lesions, whilst all of the combination groups of the two components showed a **synergistic** reduction of the lesions.

DETD **Synergism** of HMG CoA reductase inhibitors and thiazolidinedione insulin sensitizers was examined by another regression model, i.e. the regression of preformed. . .

DETD . . . observed, with a dose-dependent trend based on troglitazone. In the case of the combination of fluvastatin and troglitazone a similar **synergistic** regression of aortic lesions was observed.

CLM What is claimed is:

. . . agent selected from the group consisting of thiazolidinedione insulin sensitizers, said first and second agents being administered together in a **synergistic** mixture or individually in amounts and within such a period as to act **synergistically** together, with the proviso that, when the first agent is pravastatin, the second agent is not troglitazone and wherein the. . .

. . . and a second agent selected from the group consisting of thiazolidinedione insulin sensitizers, said first and second agents

being in **synergistic** amounts admixed or packaged separately, and wherein said HMG-CoA reductase inhibitors are selected from the group consisting of pravastatin, lovastatin,. . .
140. A pharmaceutical composition for the treatment or prophylaxis of arteriosclerosis or xanthoma, comprising, in **synergistic** amounts, a first agent selected from the group consisting of HMG-CoA reductase inhibitors and a second agent selected from the. . .

IT 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81131-70-6, Pravastatin sodium 93957-54-1, Fluvastatin 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**, BRL-49653 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 178054-38-1 187220-90-2 187220-91-3
(synergistic compn. contg. insulin sensitizer and HMG-CoA reductase inhibitor for treatment of arteriosclerosis)

L26 ANSWER 25 OF 30 USPATFULL on STN
AN 2000:161029 USPATFULL
TI Method and composition for the treatment of diabetes
IN Rieveley, Robert B., 4102 Yuculta Crescent, Vancouver, British Columbia, Canada V6N 3R5
PI US 6153632 20001128
AI US 1997-804903 19970224 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Oyen Wiggs Green & Mutala
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . efficiency that she experienced a hypoglycaemic condition. It appeared clear that there was a startling effect, and indeed perhaps a **synergistic** effect, created between the combination of insulin and the V-411 insulin sensitizer. Thus, much smaller dosages of insulin could have. . .
DETD . . . degradation effects of the gastric juices of the stomach and enzymatic action of the gut. Because of the strong or **synergistic** effect involving the combination of insulin and the insulin sensitizer, it follows that the inclusion of an insulin sensitizer in. . .
IT 56-03-1, Biguanide 98-98-6D, Picolinic acid, chromium derivs. 97322-87-7, Troglitazone 112529-15-4, Pioglitazone hydrochloride **122320-73-4**, BRL-49653 153559-49-0, LGD 1069 153559-76-3, ALRT 268 309956-37-4, MC 555
(diabetes mellitus treatment compns. contg. insulin sensitizers and antidiabetic agents)

L26 ANSWER 26 OF 30 USPATFULL on STN
AN 2000:67567 USPATFULL
TI Modulators of ob gene and screening methods therefor
IN Briggs, Michael R., Downingtown, PA, United States
Auwerx, Johan, Millionfosse, France
de Vos, Piet, Zingem, Belgium
Staels, Bart, Kraainem, Belgium
Croston, Glenn E., San Diego, CA, United States
Miller, Stephen G., San Diego, CA, United States
PA Ligand Pharmaceuticals Incorporated, San Diego, CA, United States (U.S. corporation)
PI US 6068976 20000530
AI US 1996-618100 19960319 (8)
RLI Continuation-in-part of Ser. No. US 1995-558588, filed on 30 Oct 1995,

now abandoned which is a continuation-in-part of Ser. No. US 1995-510584, filed on 2 Aug 1995, now abandoned which is a continuation-in-part of Ser. No. US 1995-418096, filed on 5 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1995-408584, filed on 20 Mar 1995, now abandoned

DT Utility
FS Granted
EXNAM Primary Examiner: Yucel, Remy
LREP Lyon & Lyon LLP
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 48 Drawing Figure(s); 21 Drawing Page(s)
LN.CNT 3662
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . to down regulate ob gene expression. Without being bound by any theory, applicant proposes that TNF and ob gene act **synergistically** to affect food intake. Inhibitors of TNF and inhibitors of ob production may act **synergistically** to relieve cachexia.
IT **122320-73-4**, BRL49653
(PPAR.gamma. agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

L26 ANSWER 27 OF 30 USPATFULL on STN
AN 2000:1892 USPATFULL
TI Combinations for diabetes
IN Whitcomb, Randall Wayne, Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 6011049 20000104
AI US 1998-189132 19981109 (9)
RLI Continuation-in-part of Ser. No. US 1997-970057, filed on 13 Nov 1997, now patented, Pat. No. US 5859037
PRAI US 1997-38224P 19970219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Ashbrook, Charles W.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 974
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . chemically related to the sulfonylureas, it routinely is utilized in combination with a sulfonylurea, and has been shown to be **synergistic** in some cases. Other biguanides can also be used.
DETD . . . atherogenic risk. It should be noted that patients with elevated triglycerides levels could potentially benefit from troglitazone treatment and provide **synergism** to the management of their dyslipidemia since elevated triglyceride levels are recognized as an independent risk factor for cardiovascular disease.
CLM What is claimed is:
. . . rosiglitazone and pioglitazone, and from about 300 mg to about 2000 mg of a biguanide antidiabetic agent, said amounts being **synergistic** in the treatment of non-insulin dependent diabetes mellitus.

4. A **synergistic** composition comprising from about 100 mg to about 1000 mg of troglitazone, from about 3 mg to about 250 mg. . .
5. A **synergistic** composition comprising from about 5 mg to about 10 mg of rosiglitazone, from about 3 mg to about 250 mg. . .

6. A **synergistic** composition comprising from about 50 mg to about 200 mg of pioglitazone, from about 3 mg to about 250 mg. . . . . and pioglitazone and from about 300 mg to about 2000 mg of a biguanide antidiabetic agent, wherein said amounts are **synergistic** for the treatment of non-insulin dependent diabetes mellitus.

. . . 2000 mg of metformin and from about 3 mg to about 250 mg of a sulfonylurea, wherein said amounts are **synergistic** for the treatment of non-insulin dependent diabetes mellitus.

. . . 2000 mg of metformin and from about 3 mg to about 250 mg of a sulfonylurea, wherein said amounts are **synergistic** for the treatment of non-insulin dependent diabetes mellitus.

. . . 2000 mg of metformin and from about 3 mg to about 250 mg of a sulfonylurea, wherein said amounts are **synergistic** for the treatment of non-insulin dependent diabetes mellitus.

IT 56-03-1D, Biguanide, derivs. 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 451-71-8, Glyhexamide 657-24-9, Metformin 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 97322-87-7, Troglitazone 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone
(combinations of glitazones, biguanides, and optional sulfonylureas for diabetes treatment)

L26 ANSWER 28 OF 30 USPATFULL on STN
AN 1999:132855 USPATFULL
TI Sulfonylurea-glitazone combinations for diabetes
IN Whitcomb, Randall Wayne, Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 5972973 19991026
AI US 1998-173911 19981016 (9)
RLI Continuation-in-part of Ser. No. US 1997-970057, filed on 13 Nov 1997, now patented, Pat. No. US 5859037
PRAI US 1997-38224P 19970219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Ashbrook, Charles W.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 733
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . atherogenic risk. It should be noted that patients with elevated triglycerides levels could potentially benefit from troglitazone treatment and provide **synergism** to the management of their dyslipidemia since elevated triglyceride levels are recognized as an independent risk factor for cardiovascular disease.
CLM What is claimed is:
. . . antidiabetic agent and about 5 mg to about 50 mg of rosiglitazone (BRL49653), said amounts of sulfonylurea and rosiglitazone being **synergistic** for the treatment of non-insulin dependent diabetes mellitus in humans.

. . . agent in combination with about 5 mg to about 50 mg of rosiglitazone, said amounts of sulfonylurea and rosiglitazone being **synergistic**

for the treatment of non-insulin dependent diabetes mellitus in humans.

. . . agent in combination with about 5 mg to about 10 mg of rosiglitazone, said amounts of sulfonylurea and rosiglitazone being **synergistic** for the treatment of non-insulin dependent diabetes mellitus in humans.

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 451-71-8, Glyhexamide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 97322-87-7, Troglitazone 111025-46-8, Pioglitazone **122320-73-4**, Rosiglitazone
(sulfonylurea-glitazone combinations for treatment of diabetes)

L26 ANSWER 29 OF 30 USPATFULL on STN
AN 1999:4694 USPATFULL
TI Sulfonylurea-glitazone combinations for diabetes
IN Whitcomb, Randall Wayne, Ann Arbor, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 5859037 19990112
AI US 1997-970057 19971113 (8)
PRAI US 1997-38224P 19970219 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Ashbrook, Charles W.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1902
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD . . . HbA.sub.1 c levels less than or equal to 8% at baseline and at 52 weeks of treatment, and establishes the **synergistic** increase in control achieved with combination therapy.
DETD . . . 500 mg of troglitazone. Such combination will be administered to an adult patient about once each day to achieve a **synergistic** glycemic control.
DETD . . . of stimulated release of insulin while ameliorating insulin resistance. The results obtained in this study provide evidence of significant and **synergistic** improvement in glycemic control of patients with very few remaining therapeutic options.
DETD . . . atherogenic risk. It should be noted that patients with elevated triglycerides levels could potentially benefit from troglitazone treatment and provide **synergism** to the management of their dyslipidemia since elevated triglyceride levels are recognized as an independent risk factor for cardiovascular disease.
DETD . . . sulfonylurea). Combination therapy of a glitazone and sulfonylurea appears to be safe and well-tolerated and can result in significant and **synergistic** improvement in glycemic control. It should be noted that patients on maximum doses of a sulfonylurea should not be switched. . .
DETD . . . and tolazamide. Still another combination provided by this invention is englitazone together with glibornuride, glyburide, or glisoxepid. These combinations produce **synergistic** glycemic control and will be utilized at doses which are **synergistic**. The **synergistic** combinations of this invention can also be utilized to treat conditions such as impaired glucose tolerance (IGT), thereby preventing or. . .
CLM What is claimed is:
. . . from about 100 mg to about 1000 mg of a glitazone antidiabetic agent, said amounts of sulfonylurea and glitazone being **synergistic**

for the treatment of non-insulin dependent diabetes mellitus in humans.

. . . agent in combination with about 100 mg to about 1000 mg of a glitazone antidiabetic agent, wherein said amounts are **synergistic** in the treatment of non-insulin dependent diabetes mellitus.

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 451-71-8, Glyhexamide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 74772-77-3, Ciglitazone 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone 118384-10-4, TA 174 **122320-73-4**, BRL 49653
(sulfonylurea-glitazone combinations for diabetes)

L26 ANSWER 30 OF 30 USPATFULL on STN
AN 1998:101666 USPATFULL
TI Treatment of arteriosclerosis and xanthoma
IN Tsujita, Yoshio, Tokyo, Japan
Horikoshi, Hiroyoshi, Kobe, Japan
Ito, Takashi, Kobe, Japan
PA Sankyo Company, Limited, Tokyo, Japan (non-U.S. corporation)
PI US 5798375 19980825
AI US 1996-676090 19960702 (8)
PRAI JP 1995-167291 19950703
DT Utility
FS Granted
EXNAM Primary Examiner: Criares, Theodore J.
LREP Frishauf, Holtz, Goodman, Langer & Chick, Esq.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1158
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . insulin sensitizers (for example troglitazone, pioglitazone, englitazone, BRL-49653, 5-(4-{2-[1-(4-2'-pyridylphenyl)ethylideneaminooxy]-ethoxy}benzyl)thiazolidine-2,4-dione, 5-{4-(5-methoxy-3-methylimidazo[5,4-b]pyridin-2-yl-methoxy)benzyl}thiazolidine-2,4-dione or its hydrochloride, 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione, 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]-thiazolidine-2,4-dione and 5-[4-(5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-ylmethoxy) benzyllthiazolidine-2,4-dione) exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the. . .
SUMM . . . the application of a combination of one or more HMG-CoA reductase inhibitors with one or more insulin sensitizers exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the. . .
SUMM It is a further, and more specific object of the invention to provide such a combination exhibiting a **synergistic** effect.
SUMM . . . consisting of insulin sensitizers, said first and second agents being administered together or within such a period as to act **synergistically** together.
DETD At present, the experimental evidence seems to us to suggest that the **synergistic** effect arises from an interaction between the modes of action of the two classes of compounds, the HMG-CoA reductase inhibitors. . .
DETD . . . insulin resistance-improving agents. According to the invention, a combination of the HMG-CoA reductase inhibitor and the

insulin sensitizer exhibits a **synergistic** effect in comparison with the application of the respective components alone, as shown below. Interestingly, such **synergism** appears to occur even if the compounds of the two classes do not always exist simultaneously in the body. That is, the **synergistic** effect may be observed even when the concentration of one of the compounds of the two classes in the blood. . . . from the previous administration of the other compound, and the effects of the two compounds operate together in a favourable **synergistic** manner. It is, of course, obvious that it may well be convenient to administer the two compounds simultaneously in clinical. . . . separately in the form of single doses. As described above, since the compounds of the two classes exhibit together a **synergistic** effect, they may be administered almost simultaneously or at suitable intervals. The maximum interval acceptable for administering the compounds of the two classes in order to achieve the **synergistic** effect of the present invention may be confirmed by clinical practice or by experiments using animals.

DETD . . . their original uses, that is as antihyperlipidemic and antidiabetic agents. Their doses are further lowered to some extent by the **synergistic** effect due to the combination of the compounds of the two classes. For example, where pravastatin and troglitazone are used. . .

DETD The present invention is further illustrated by the following Examples, which demonstrate the enhanced activity achieved by the **synergistic** combination of the present invention. In addition, the subsequent Formulations illustrate the pharmaceutical formulations which may be prepared and the. . .

DETD . . . (which received a combination of both agents) and group B (which received pravastatin alone). In contrast, there was observed clear **synergism** in the percent lesion area ratio (lesion area/total artery area in %) by comparing Group D (combination treatment) with Groups B and C (single agent treatment) as shown above. **Synergism** was observed in preventing coronary stenosis in respect of the left anterior descending artery, the left circumflex artery and the right coronary artery. Development of xanthoma on the digital joints was entirely prevented in Group D, thus demonstrating clear **synergism**.

DETD . . . reductase inhibitor and an insulin sensitizer with the groups administered the active agent alone, the combination of both active agents **synergistically** prevented progression of the arteriosclerosis, particularly of the thoracic aorta. These results could not be imagined from the state of. . .

DETD . . . results are that the two combinations of pravastatin, a HMG-CoA reductase inhibitor, and one of the thiazolidinedione insulin sensitizers exhibit **synergistic** effects on the treatment of atherosclerosis and on the occurrence of xanthoma.

DETD **Synergism** of HMG CoA reductase inhibitors and thiazolidinedione insulin sensitizers were examined on the regression of established atherosclerotic lesions in the. . .

DETD . . . showed no or little reduction of the lesions, whilst all of the combination groups of the two components showed a **synergistic** reduction of the lesions.

DETD **Synergism** of HMG CoA reductase inhibitors and thiazolidinedione insulin sensitizers was examined by another regression model, i.e. the regression of preformed. . .

DETD . . . observed, with a dose-dependent trend based on troglitazone. In the case of the combination of fluvastatin and troglitazone a similar **synergistic** regression of aortic lesions was observed.

CLM What is claimed is:

. . . second agent selected from the group consisting of insulin sensitizers, said first and second agents being administered together in a **synergistic** mixture or individually in amounts and within

such a period as to act **synergistically** together; wherein said HMG-CoA reductase inhibitor is pravastatin and said insulin sensitizer is troglitazone.

IT 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 81131-70-6, Pravastatin sodium 93957-54-1, Fluvastatin 97322-87-7, Troglitazone 109229-58-5, Englitazone 111025-46-8, Pioglitazone **122320-73-4**, BRL-49653 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 178054-38-1 187220-90-2 187220-91-3
(synergistic compn. contg. insulin sensitizer and HMG-CoA reductase inhibitor for treatment of arteriosclerosis)

=> D HIS

(FILE 'HOME' ENTERED AT 14:53:40 ON 22 JUL 2003)

FILE 'USPATFULL' ENTERED AT 14:53:52 ON 22 JUL 2003
L1 864 S THIAZOLIDINE-2,4-DIONE
L2 172 S BENZYL(1W)THIAZOLIDINE-2,4-DIONE
L3 105 S ETHOXY(1W)BENZYL(1W)THIAZOLIDINE-2,4-DIONE
L4 87 S L3 AND PYRIDYL
L5 0 S S ;4 AND N(1W)METHYLEND
L6 73 S L4 AND N(1W)METHYL
L7 72 S L6 AND AMINO
L8 65 S L7 AND 2(1W) PYRIDYL
L9 56 S L8 (1P) INSULIN

FILE 'REGISTRY' ENTERED AT 15:02:41 ON 22 JUL 2003
L10 0 S BNL49653/CN
L11 0 S BNL 49653/CN
L12 1 S BRL 49653/CN

FILE 'USPATFULL' ENTERED AT 15:05:33 ON 22 JUL 2003
L13 285 S ROSIGLITAZONE (1P) INSULIN
L14 0 S L13 AND PD<1994
L15 0 S L13 AND PD<1995
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L22 148 S 122320-73-4/RN
L23 0 S L22 AND INSULIN/CLS
L24 78 S L22 AND INSULIN/CLM
L25 3 S L24 AND PD<1999
L26 30 S L22 AND SYNERGIS?

=> D L26 1-30 TI, AB

L26 ANSWER 1 OF 30 USPATFULL on STN
TI Combination of organic compounds
AB The invention relates to a combination, such as a combined preparation or pharmaceutical composition, respectively, comprising the renin inhibitor of formula (I) or a pharmaceutically acceptable salt thereof and at least one antidiabetic agent.

L26 ANSWER 2 OF 30 USPATFULL on STN
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and alpha glucocidase inhibitor
AB A method for the treatment of diabetes mellitus and conditions

associated with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amount of an insulin sensitiser, an insulin secretagogueand an alpha glucosidase inhibitor antihyperglycaemic agent, to a mammal in need thereof; and composition for use in such method.

L26 ANSWER 3 OF 30 USPATFULL on STN
TI Method of treating metabolic disorders especially diabetes, or a disease or condition associated with diabetes
AB The invention relates to a combination, such as a combined preparation or pharmaceutical composition, respectively, which comprises nateglinide (I) ##STR1##

or repaglinide and at least one other antidiabetic compound selected from the group consisting of thiazolidinedione derivatives (glitazones), sulfonyl urea derivatives and metformin for simultaneous, separate or sequential use in the prevention, delay of progression or treatment of diseases, especially metabolic disorders and in particular type 2 diabetes and diseases and conditions associated with diabetes; to a composition, respectively, which comprises nateglinide and a pharmaceutically acceptable carrier and to a process of making such composition; the use of such combination or composition for the preparation of a medicament for the prevention, delay of progression or treatment of metabolic disorders; a method of prevention, delay of progression or treatment of diseases in warm-blooded animals; the use of such combination or composition for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body weight; and to a method of improving the bodily appearance of a warm-blooded animal.

L26 ANSWER 4 OF 30 USPATFULL on STN
TI Combinations comprising a beta-agonist and a further antidiabetic agent
AB A method for the treatment of diabetes mellitus and conditions associated with diabetes mellitus in a mammal such as a human, which method comprises administering an effective, non-toxic and pharmaceutically acceptable amount of a beta agonist and another antidiabetic agent, to a mammal in need thereof.

L26 ANSWER 5 OF 30 USPATFULL on STN
TI Drug comprising combination
AB A TNF-.alpha. inhibitor comprising an insulin sensitizer in combination with an HMG-CoA reductase inhibitor is useful as an agent for the prophylaxis or treatment of an inflammatory disease and the like.

L26 ANSWER 6 OF 30 USPATFULL on STN
TI Combined use of derivatives of GLP-1 analogs and PPAR ligands
AB The present invention provides methods and compositions for treatment and/or prevention of type 1 and type 2 diabetes, dyslipdemia, impaired glucose tolerance, insulin resistance, obesity, and beta-cell apoptosis, as well as methods for increasing the size and number of beta-cells in a subject and/or stimulating beta-cell proliferation, which comprise administering both a stable GLP-1 analogue and a non-thiazolidinedione PPAR ligand.

L26 ANSWER 7 OF 30 USPATFULL on STN
TI Novel remedies with the use of beta 3 agonist
AB Provided is a therapeutic agent comprising at least one member selected from the group consisting of an anticholinergic agent, a monoamine reuptake inhibitor, a lipase inhibitor, a selective serotonin reuptake inhibitor, insulin, an insulin secretagogue, biguanide, an .alpha.-glucosidase inhibitor, an insulin resistance improving agent, a HMG-CoA reductase inhibitor, an anion exchange resin, a clofibrate type drug and a nicotinic acid type drug, and a compound having a .beta.3

agonist activity. The .beta.3-agonist has an activity of inhibiting dysuria. Further, when used together with a remedy for dysuria such as propiverine, oxybutynin hydrochloride or tolterodine, it exerts an enhanced anti-dysuria effect. When used together with an antiobestic agent such as sibutramine or orlistat, it exerts an enhanced antiobestic effect. When used together with an antidiabetic agent such as insulin, glibenclamide, acarbose or rosiglitazone, it exerts an enhanced antidiabetic effect. When used together with an antilipemic agent such as bezafibrate or pravastatin, it exerts an enhanced antilipemic effect.

L26 ANSWER 8 OF 30 USPATFULL on STN
TI Combined use of derivatives of GLP-1 analogs and PPAR ligands
AB The present invention provides methods and compositions for treatment and/or prevention of type 1 and type 2 diabetes, dyslipdemia, impaired glucose tolerance, insulin resistance, obeity, and beta-cell apoptosis, as well as methods for increasing the size and number of beta-cells in a subject and/or stimulating beta-cell proliferation, which comprise administering both a stable GLP-1 analogue and a non-thiazolidinedione PPAR ligand.

L26 ANSWER 9 OF 30 USPATFULL on STN
TI Methods and compositions for the treatment of alopecia and other disorders of the pilosebaceous apparatus
AB Insulin sensitivity increasing substances (ISIS), including but not limited to D-chiro-inositol, thiazolidinedione and derivatives, and biguanides, are useful in the treatment of hair loss and other disorders of the pilosebaceous apparatus (hirsutism, acne, etc.) associated with conditions of excess insulin and/or insulin resistance. The treatment comprises administering to a mammal, such as a human, at least one ISIS either alone or in combination with at least one agent, such as an androgen receptor blocker (ARB) and/or a steroid enzyme inhibitor or inducer (STI). Additionally, an activity enhancing agent may be included for topical administration.

L26 ANSWER 10 OF 30 USPATFULL on STN
TI Differentiating agents for the treatment of inflammatory intestinal diseases
AB A method for decreasing the inflammation associated with a chronic inflammatory intestinal condition in a patient is provided wherein the patient is administered an effective amount of a differentiating agent.

L26 ANSWER 11 OF 30 USPATFULL on STN
TI Peroxisome proliferator-acitvated receptor gamma ligand eluting medical device
AB Implantable medical devices having an anti-restenotic coatings are disclosed. Specifically, implantable medical devices having coatings of peroxisome proliferator-activated receptor gamma (PPAR.gamma.) agonists are disclosed. The anti-restenotic PPAR.gamma. ligands include thiazolidinedione compounds including ciglitazone. The anti-restenotic medial devices include stents, catheters, micro-particles, probes and vascular grafts. The medical devices can be coated using any method known in the art including compounding the thiazolidinedione with a biocompatible polymer prior to applying the coating. Moreover, medical devices composed entirely of biocompatible polymer-thiazolidinedione blends are disclosed. Additionally, medical devices having a coating comprising at least one thiazolidinedione in combination with at least one additional therapeutic agent are also disclosed. Furthermore, related methods of using and making the anti-restenotic implantable devices are also disclosed.

L26 ANSWER 12 OF 30 USPATFULL on STN
TI Use of RAR antagonists as modulators of hormone mediated processes

AB In accordance with the present invention, it has been discovered that retinoic acid receptor (RAR) antagonists are capable of modulating processes mediated by other members of the steroid/thyroid hormone receptor superfamily, including permissive receptors such as PPARs (e.g., PPAR.alpha., PPAR.delta. and PPAR.gamma.). Indeed, it has been discovered that RAR antagonists, in combination with agonists for members of the steroid/thyroid hormone receptor superfamily, are capable of inducing and/or enhancing processes mediated by such members.

L26 ANSWER 13 OF 30 USPATFULL on STN
TI PAX8-PPARgamma nucleic acid molecules and polypeptides and uses thereof
AB An oncogene designated PAX8-PPAR.gamma.1 contains a PAX8 coding region fused to PPAR.gamma. coding region. Molecular characterization of PAX8-PPAR.gamma.1 molecules provides nucleotide and amino acid sequences useful for detection and treatment of certain tumors, particularly thyroid follicular carcinomas.

L26 ANSWER 14 OF 30 USPATFULL on STN
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and alpha glucocidase inhibitor
AB A method for the treatment of diabetes mellitus and conditions associated with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amount of an insulin sensitizer, an insulin secretagogue and an alpha glucosidase inhibitor antihyperglycaemic agent, to a mammal in need thereof; and composition for use in such method.

L26 ANSWER 15 OF 30 USPATFULL on STN
TI Metforimin-containing compositions for the treatment of diabetes
AB Compositions and methods using same for the treatment of diabetes its sequelae and pre-diabetic conditions are provided. Invention compositions include the anti-diabetic agent metformin, and bioavailable sources of one or more of chromium, vanadium and magnesium. Also provided are pharmaceutical agents containing invention compositions and methods for administering such agents.

L26 ANSWER 16 OF 30 USPATFULL on STN
TI Combination therapeutic compositions and method of use
AB The present invention provides pharmaceutical compositions and methods for the treatment of diabetes mellitus using combination therapy. The compositions relate to a compound of Formula I and an antidiabetic agent such as sulfonylureas, biguanides, glitazones, .alpha.-glucosidase inhibitors, potassium channel antagonists, aldose reductase inhibitors, glucagon antagonists, activators of RXR, insulin therapy or other anti-obesity agent. The methods include the administration of the combination of compound of Formula I with antidiabetic agent where the two components are delivered in a simultaneous manner, where the compound of Formula I is administered first, followed by the antidiabetic agent, as well as wherein the antidiabetic agent is delivered first followed by the compound of Formula I.

L26 ANSWER 17 OF 30 USPATFULL on STN
TI Treatment of diabetes with thiazolidinedione, insulin secretagogue and diguanide
AB A method for the treatment of diabetes mellitus and conditions associated with diabetes mellitus in a mammal, which method comprises administering an effective non-toxic and pharmaceutically acceptable amount of an insulin sensitiser, an insulin secretagogue and a biguanide antihyperglycaemic agent, to a mammal in need thereof; and composition for use in such method.

L26 ANSWER 18 OF 30 USPATFULL on STN

TI **Synergistic** effect of a sulfonylurea and/or non-sulfonylurea Kchannel blocker, and a phosphodiesterase 3 type inhibitor

AB The present invention provides methods of treating non-insulin dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance, the methods comprising the step of administering to a patient having or at risk of having non-insulin dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance a **synergistic** amount of: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; and 2) a cAMP phosphodiesterase type 3 inhibitor. The present invention also provides kits and pharmaceutical compositions that comprise: 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; and 2) a cAMP phosphodiesterase type 3 inhibitor. The present invention also relates to kits and pharmaceutical compositions that comprise 1) a sulfonylurea, a non-sulfonylurea K.sup.+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K.sup.+ ATP channel blocker; 2) a cAMP phosphodiesterase type 3 inhibitor; and 3) an additional compound useful for the treatment of non-insulin dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance.

L26 ANSWER 19 OF 30 USPATFULL on STN

TI METHODS AND PHARMACEUTICAL COMPOSITIONS FOR INHIBITING TUMOR CELL GROWTH

AB The present invention is based on the finding that activation of PPAR.gamma. plays a key role in inducing growth arrest and differentiation of certain actively proliferating cells. We show that administration of PPAR.gamma. agonists, such as thiazolidinedione ligands (TZDs), is effective both in vitro and in vivo at inhibiting the proiferation of such cells.

L26 ANSWER 20 OF 30 USPATFULL on STN

TI Methods of treating liver disorders and disorders associated with liver function

AB Methods of treating liver inflammatory condition, disease or disorder are provided. Methods include administering amounts of a PPAR.gamma. agonist sufficient to ameliorate the inflammatory condition, disease or disorder. Methods of treating conditions associated with excess or undesirable cholesterol levels or decreased HDL levels or decreased CYP7A expression are also provided. Methods include administering amounts of a PPAR.gamma. agonist sufficient to decrease cholesterol levels or increase HDL levels or CYP7A expression.

L26 ANSWER 21 OF 30 USPATFULL on STN

TI Method of inhibiting angiogenesis

AB Angiogenesis is inhibited and the growth of tumors is treated by administering an effective amount of a PPAR gamma ligand/agonist, optionally with an RXR receptor ligand.

L26 ANSWER 22 OF 30 USPATFULL on STN

TI Method and composition for the treatment of diabetes

AB This invention is directed to a novel method and composition for the treatment of diabetes mellitus (Type I, Impaired Glucose Tolerance ["IGT"] and Type II). More specifically, this invention pertains to a novel method of treating diabetes mellitus by incorporating a therapeutic amount of one or more insulin sensitizers along with one or

more of an orally ingested insulin, an injected insulin, a sulfonylurea, a biguanide or an alpha-glucosidase inhibitor for the treatment of diabetes mellitus.

L26 ANSWER 23 OF 30 USPATFULL on STN
TI Methods and pharmaceutical compositions for inhibiting tumor cell growth
AB A method for inhibiting proliferation of a PPAR .gamma.-responsive hyperproliferative cell which comprises the step of contacting the cell with (I) an inhibitory amount of a PPAR.gamma. agonist and (II) a MAP kinase inhibitor is disclosed. A method for treating or prophylactically preventing in an animal subject a disorder characterized by unwanted proliferation of PPAR.gamma.-responsive hyperproliferative cells which comprises administering to the subject (I) an inhibitory amount of a PPAR.gamma. agonist and (II) a MAP kinase inhibitor is also disclosed. Pharmaceutical compositions comprising a therapeutically effective amount of a PPAR.gamma. agonist and a MAP kinase inhibitor are disclosed for use in the methods.

L26 ANSWER 24 OF 30 USPATFULL on STN
TI Treatment of arteriosclerosis and xanthoma
AB A combination of one or more HMG-CoA reductase inhibitors (for example pravastatin, lovastatin, simvastatin, fluvastatin, rivastatin or atorvastatin) with one or more insulin sensitizers (for example troglitazone, pioglitazone, englitazone, BRL-49653, 5-(4-(2-[1-(4-2'-pyridylphenyl)ethylideneaminooxy]ethoxy)benzyl)thiazolidine-2,4-dione, 5-{4-(5-methoxy-3-methylimidazo[5,4-b]pyridin-2-ylmethoxy)benzyl}thiazolidine-2,4-dione or its hydrochloride, 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione, 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione and 5-[4-(5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione) exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the combination alone.

L26 ANSWER 25 OF 30 USPATFULL on STN
TI Method and composition for the treatment of diabetes
AB This invention is directed to a novel method and composition for the treatment of diabetes mellitus (Type I, Impaired Glucose Tolerance ["IGT"]and Type II). More specifically, this invention pertains to a novel method of treating diabetes mellitus by incorporating a therapeutic amount of one or more insulin sensitizers along with one or more of an orally ingested insulin, an injected insulin, a sulfonylurea, a biguanide or an alpha-glucosidase inhibitor for the treatment of diabetes mellitus.

L26 ANSWER 26 OF 30 USPATFULL on STN
TI Modulators of ob gene and screening methods therefor
AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a method for identifying and screening for agents useful for the treatment of diseases and pathological conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other control regions of the ob gene. A PPAR.gamma. agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body weight loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, diabetes, hypertension, cardiovascular diseases and infertility.

L26 ANSWER 27 OF 30 USPATFULL on STN
TI Combinations for diabetes

AB Combinations of a glitazone antidiabetic agent and a biguanide antidiabetic agent, and optionally a sulfonylurea antidiabetic agent, are useful for treating diabetes mellitus and improving glycemic control.

L26 ANSWER 28 OF 30 USPATFULL on STN
TI Sulfonylurea-glitazone combinations for diabetes
AB Combinations of a sulfonylurea antidiabetic agent and a glitazone antidiabetic agent are useful for treating diabetes mellitus and improving glycemic control.

L26 ANSWER 29 OF 30 USPATFULL on STN
TI Sulfonylurea-glitazone combinations for diabetes
AB Combinations of a sulfonylurea antidiabetic agent and a glitazone antidiabetic agent are useful for treating diabetes mellitus and improving glycemic control.

L26 ANSWER 30 OF 30 USPATFULL on STN
TI Treatment of arteriosclerosis and xanthoma
AB A combination of one or more HMG-CoA reductase inhibitors (for example pravastatin, lovastatin, simvastatin, fluvastatin, rivastatin or atorvastatin) with one or more insulin sensitizers (for example troglitazone, pioglitazone, englitazone, BRL-49653, 5-(4-{2-[1-(4-2'-pyridylphenyl)ethylideneaminooxy]-ethoxy}benzyl)thiazolidine-2,4-dione, 5-{4-(5-methoxy-3-methylimidazo[5,4-b]pyridin-2-yl-methoxy)benzyl}thiazolidine-2,4-dione or its hydrochloride, 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione, 5-[4-(1-methylbenzimidazol-2-ylmethoxy)benzyl]-thiazolidine-2,4-dione and 5-[4-(5-hydroxy-1,4,6,7-tetramethylbenzimidazol-2-ylmethoxy) benzyllthiazolidine-2,4-dione) exhibits a **synergistic** effect and is significantly better at preventing and/or treating arteriosclerosis and/or xanthoma than is either of the components of the combination alone.